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SOME PROBLEMS OF SOVIET MEDICAL PRACTICE: A SOCIOLOGICAL APPROACH*

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SOCIOLOGY views the work of the physician as part of the general division of labor in society and attempts to relate his functions to other aspects of the social order.[1, 2] Of particular interest in this respect is the problem of the issuance by the physician of sickness certificates as valid excuses to obtain relief from certain obligations or to by-pass certain regulations.

It is a general premise, in a "rational" system of medicine, that true illnesses or injuries are not the result of the motivation of the patient, and that he must not be held morally or legally accountable for what he does or fails to do on account of illness or injury. To be a "patient," therefore, not only entails certain obligations, such as obeying the doctor's orders and "making an effort to get well," but also relieves the person of certain duties and endows him with certain privileges that he would not get under "normal" circumstances. But, as Boisseau[3] remarks:

> If it is true that the first man who saw his neighbor suffer must have sought ways to help him, it is also certain that seeing the care lavished upon the sick, the deference that was granted them, the advantages that their patient status conferred upon them, the idea of simulation must not have been late in arising.

Certification of illness (or self-certification) cannot be left, in the majority of cases, to the person who claims the patient role. It is the physician, then, as the only person technically qualified to do so, who must "legitimize" sickness in the eyes of society. This also means that abuses of the medical system will be oriented toward deceiving the physician into believing one's sickness or injury to be independent of one's *conscious* motivation whereas it *actually is not*. This introduces a complicating element in the sense that the classic assumption that the person who comes to the physician must necessarily be sick (independently of motivation) is no longer tenable; the opposite assumption may, in certain cases, be just as valid. This has, in turn, important implications and consequences for both the physician and the "genuine" patient. Some of these implications are taken up in detail below.

It is the contention presented here that claims for medical exemptions on nonmedical grounds do not constitute a random phenomenon, solely dependent on the personalities of the patients seen by the physician, but are rather the end product of a complex of social, cultural and economic forces. (A man stranded alone on an island does not malinger.) It is further hypothesized that a relatively high rate of such claims is an index of social malintegration and malaise, which the physician, through a judicious use of the medical dispensation in nonmedical cases, may, to some extent, reduce. An inquiry into some aspects of Soviet medical practice affords an opportunity to test the validity of this hypothesis.

THE SOVIET MEDICAL WORLD

Generally speaking, access to the Soviet medical world has been denied Western observers, and consequently little is known about its organization or even its technics.[4] During World War II, when sympathy toward the Soviet Union ran high, organizations such as the American-Soviet Medical Society and its journal, the *American Review of Soviet Medicine*, hoped that medicine, a field traditionally removed from political considerations, might pave the way to peaceful international co-operation in the postwar years. Unfortunately, this hope has not been realized, and at this writing Soviet and Western physicians are more isolated from each other than they have ever been. The *Review of Soviet Medicine* stopped publication in 1948, not because Soviet materials were not forthcoming but because of the general political situation.[5]

In the absence of direct, quantitative and objective data on the Soviet world one must fall back on other sources of information. One such source, avail-

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able only since the end of World War II, consists of the many former Soviet citizens who failed to return home from Western Europe after the end of hostilities. Although the reasons for defection are many and too complicated to be examined here,[8] the former Soviet citizens remain, in many cases, the only source of eye-witness information on Soviet Russia. An a priori and unqualified refusal to listen to these persons is clearly untenable under the present conditions of scarcity of knowledge. Whereas the Displaced Persons do not constitute a random or representative sample of the Soviet population, they can with the proper precautions, reserve and due qualifications give the West valuable (and otherwise unobtainable) insight into some of the workings of the Soviet world. This insight is, of course, indirect, qualitative and subjective. Its accuracy, reliability and validity are the result of three elements: the internal consistency of the Displaced Persons sample; general knowledge of societies in general and of Soviet society in particular, confirmed and documented by reports of Western observers; and the official *Soviet* sources themselves, many of which are available in the West. It is only in this perspective that an approach to the study of Soviet society may be more than mere speculation and wishful thinking.

Methods

A general investigation into the nature and functioning of the Soviet social system was undertaken by a team of social scientists affiliated with the Harvard Russian Research Center. Approximately 2500 former Soviet citizens were either interviewed or asked to fill in detailed questionnaires on certain aspects of Soviet life. In the course of this study 21 former Soviet physicians were intensively interviewed; in addition 1600 Displaced Persons filled in questionnaires on their reactions to the Soviet type of medicine: finally, research was carried on in the official Soviet sources, primarily in *Meditsinski Rabotnik* [*The Medical Worker*] the semi-weekly organ of the Ministry of Health for the USSR. This paper presents certain findings concerning the role of the physician in Soviet society.

Claims for Medical Exemptions

Generally speaking, Soviet physicians distinguished three types of claims for medical excuses on nonmedical grounds. They were as follows: malingering; direct requests for the medical certificate, with or without an attempt to motivate the physician by arousing his sympathy; or requests for the medical certificate by genuine patients without request for medical attention (residual type).

Malingering

Malingering is not, of course, a phenomenon peculiar to Soviet medicine. Physicians have met it from the earliest days of medicine and are still faced with it in institutional, military, insurance and compensation claims, and in certain aspects of legal medicine.[7-11] There has been until now, however, little evidence that malingering was a problem that concerned the "workers' state." If the evidence given by the physicians interviewed is any indication (an attempt will be made later to confirm it), malingering is an issue that also confronts the Soviet physician in his daily practice, at least at the dispensary level where medical certificates are delivered. For example, a Ukrainian doctor[12] who finished her medical training in 1937 had this to say on the problem:

> It was hell...I still have nightmares about it. Many of the malingerers appeared when the law on tardiness came into effect. A good 50% of the cases at the Railroad Clinic where I worked were fakers...there were people who overslept and came late to work. People had to stand in line after shifts and work and cook...life was very hard...sleep was a dead-man's sleep and it was hard to get up in the morning. As soon as he sees he is late he will go to the doctor. You will think of some disease to excuse him.

A Georgian physician, who was chief of clinic,[13] reported on the same subject as follows:

> Georgia is not very large and always has been agricultural. When industrialization started the peasants went into the factories as it was better than entering collective farms. But the small peasant household remained with its little garden plot. And in the spring you must cultivate this plot. And as soon as spring starts and we all knew it, all the patients try to fake illness. And even if a man had a grippe and you gave him 5 days off, a doctor who would check at his home would not find him there because he went to the village. . . the socialized system of medicine is not bad, but it is the entire system which is bad, which does not give the people enough food nor interest in their work.

Guarded references to the malingering problems may be gathered in the medical journals. For example, in an article entitled "An Ideological Sketch of the Soviet Physician," S. Tikhodeev[14] addresses himself to what the Soviet doctor should be like:

> [In a dispensary the doctor who] uses formalistic methods can find in every individual he examines symptoms of pathological processes; he can label these as "hypertonic" or "vegeto-neurotic." Such "humanism" has no connection with reality, it has no scientific basis. The Soviet doctor must sift from the total mass of virtually healthy individuals these few who are really sick and need immediate medical attention ...working in a factory dispensary the physician could deprive production of a great many workers, if he were to approach the problem only from the viewpoint of the delivery of sick certificates. (How shall we solve the "problem": not give the certificate and consider the patients as malingerers or aggravators, or on the contrary give them an unlimited number out of "humane" considerations?)

In another case, the son of a patient wrote to the editor of *The Medical Worker* that his mother, who had severe pains in the region of the liver, had been hospitalized in the clinic of a Professor Voronov. While she was there she received no treatment, and her complaints only threw the Professor into a state of unexplainable exasperation: "She is malingering," yelled Voronov, addressing the writer. He further relates that after his mother was released she then went into another clinic, where her trouble was diagnosed, an operation was performed and she quickly recovered.[15]

Further, confirmation of the existence of Soviet malingering was gathered in the questionnaires. More than 600 former Soviet citizens were asked whether they thought many people faked illness in the Soviet Union to escape obligations. Of the 569 who answered the question, 256 answered in the affirmative, and 313 in the negative. They were then asked whether — and, if so, why — they had ever faked illness in the Soviet Union. Although only 20 per cent answered that they had simulated illness (perhaps the phrasing was unfortunate in that it asked admission of an irregular act), the reasons given for engaging in such behavior were varied. They could be divided into two general groups: to *avoid* certain undesirable things, such as unpleasant work, military service and punishment for minor infractions of the law; and to *obtain* certain desirable things, such as a better, different job, rest and leisure time. Other reasons given were as follows: "I did not want to be evacuated with the Reds" (when the Germans invaded the Soviet Union); "to obtain time to attend to the children" (by a woman collective farmer); "to avoid going to a demonstration"; "to avoid being arrested"; "to arrange urgent family affairs"; "to obtain a 1,000-kilometer transfer to be with my relatives"; "to stand in line to buy a coat and shoes"; "I did it only in a concentration camp because I was there without adequate clothing and shoes."

The respondents were also asked whether they had heard or knew of any methods of simulating illness and if so to indicate one or two ways of going about it. There were more than 200 responses, which ranged from the artificial production of fever, to methods for increasing the heart beat, complaints difficult to check, self-inflicted wounds and the retarding of healing (particularly in extreme situations such as Army service or concentration-camp life) and, finally, simulation of nervous diseases, which was least in frequency. One person indicated "soaking a thread in kerosene and its passing through the skin with a needle." Another wrote that one should pierce the cheeks and blow water through them and "this will cause swelling." Still another stated that many simulated sciatica pains: "After recovering from this illness the patient knew the symptoms well and easily and repeatedly received [medical] excuses." Another reported that "they irritated the skin by rubbing it with garlic or produced burns with cigarettes. At best we introduced a hair under the skin, but many cases ended in prison." A woman indicated that one of her friends was allergic to pyramidon:

> When she badly wanted a rest she swallowed two pills half an hour before going to the doctor. This caused a big, red rash on her face, her back and her breast. Usually she got two days' exemption from work.

Although, again, the sample is not claimed to be typical, there is thus ground to believe in the existence of a malingering "folklore" or culture in Soviet society.

Malingerers, in any large numbers, have several implications for medical practice. First of all, the physician begins to suspect that every claimant for medical attention may be trying to deceive him. One is reminded, for example, of the humorous (though fictional) account in *The Good Soldier Schweik*, in which every sick soldier was considered, on principle, a malingerer, and particularly of the one who was "dying of consumption, pretending he had tuberculosis." Indeed, physicians who have written on this subject point to the great danger and injustice of mistaking a sick person for a malingerer.

This element of suspicion destroys the mutual trust between doctor and patient that is of paramount importance for therapy.[16-18] Secondly, the malingerers force the really sick persons to *convince* the physician they are *not* shamming. As one interviewed physician declared: "...every patient who was sick and knew about fakers tried to aggravate his case in order to receive the medical treatment to which he was entitled."[19] Finally they overload medical facilities and reduce the medical care available to the sick population.

Direct Requests for the Medical Certificate

Although malingering remains the most universally used method of attempting to obtain a medical certificate, there are additional ways in which medical dispensations may be obtained. One of these consists in a direct appeal to the sympathy of the physician.

It may be true, though not often enough appreciated, that the role of the physician does not limit itself to the treatment of the sick organism. The physician addresses himself to a total human being, and influences, by his behavior (his art) as well as his technical skill, the recovery of his patient. There was, for example, among the Babylonians, the Jews, the Greeks and the Romans no great distinction between medical and priestly functions.[20] To this day the Catholic Church maintains shrines for which miraculous cures are claimed. There is, for instance, at the shrine at Lourdes (France), a medical bureau where claims for cures are verified by physicians.[21] Finally, an exclusive preoccupation with the biologic aspect of illness was partly responsible, in the nineteenth century, for the rise of such movements as Christian Science, which completely denied the biologic approach, and for health cults such as homeopathy, Thomsonianism, osteopathy, hydropathy and Grahamism.[22] The need for a sensitive physician is particularly acute in highly secularized societies such as the Soviet Union (and the United States), where he tends perforce to assume some of the priestly functions and is expected to lend a sympathetic ear to those who need his assistance. In many cases refusal to give help would be the practi-

cal equivalent of imposing suffering, a proposition that is foreign to all the canons of medicine, Soviet or Western. As one physician related in an interview: "How do you think we felt when women came to us, crying, begging, 'comrade doctor, give me just one day off. I want to go to my mother's in the village and get some food for my starving children.' "[23] And a gynecologist reported that an old woman asked for a certificate of a bad heart so that her son, who had been sent on a work project to Siberia and had not been home in ten years, could get permission to come and see her:

> At that moment she burst into tears. This is another conflict situation between your professional conscience and human feelings. You witnessed the terrible situation of those people, and you said to yourself "I must help this person. I cannot obey the regulations."[24]

Requests for help have some of the following implications. First of all the physician is requested, point blank, to affix his name to a statement that is known to be untrue and may make him a partner in crime either *de facto* or *de jure* or both. In view of the severity of Soviet laws this may have dangerous consequences for the physician. At the same time, such requests introduce an element of *moral* evaluation, which then tends to spread to all patient-doctor relations, in which the main question that the doctor seeks to answer is no longer "*What* is *wrong* with this person?" but rather "Does he or does he not deserve a medical excuse?" or "Is he or is he not trying to fool me with a pathetic but exaggerated and untrue story?" This tends to destroy the traditional *neutrality* of the patient-doctor relation (exclusive concern with problems of health independently of moral and other judgments) and is, in the long run, prejudicial to effective medical practice. (This absence of moral judgment and standards seems to be the prerequisite of successful medical practice.[17]) A Soviet physician,[18] writing on this subject in *The Medical Worker* noted that ". . . when speaking with a patient we must eliminate every value judgement. . ." This may also tend to irritate and frustrate the physician, because he must make moral decisions, a function for which he does not have the training or preparation that a priest, for example, has. Finally his inability, in many cases, to grant help may only highlight his own powerlessness.

Requests for the Medical Certificate without Medical Treatment

There is finally a third and residual category of claimants for the medical certificate, consisting of persons who come to the dispensary physician and ask for a certificate while they seek medical treatment elsewhere or, in other words, consult a physician privately. It should be noted that private practice, although heavily taxed, is not forbidden by law. Schedules of taxes for private medical practice were published as late as 1946.[25] In this respect the German occupation of Soviet territory almost provided a controlled experiment. It appears that as soon as Soviet authorities disappeared, almost every physician opened up private practice.[26] It thus seems that unless socialized medicine can exactly duplicate, in this sphere, the private patient-doctor relation there will always be a tendency, on the part of the patient, for the "little extra" that is of such great importance in situations of crisis. (The certificates are required, of course, not only to escape certain provisions of the law but also to draw disability pensions and sickness insurance.)

This went so far that in certain cases a physician, calling at the home of a patient, would ask him whether he wanted an examination and treatment or *only* the certificate, in which case he would ask the patient for the diagnosis established by the privately consulted physician. Since he had many calls to make he would not mind the saving of time and effort. Or as one doctor[27] put it;

> If you need a certificate you go to the dispensary doctor, but if you have a couple of roubles you go to a private doctor. The young lady physician who delivers the certificate is not a doctor in the eyes of the patient. She is a State employee who delivers the necessary papers.

Under these circumstances, the original function of the physician (treatment of patients) has completely disappeared and has been replaced by the secondary function (issuance of medical certificate). This means that the physician has entirely lost the mission for which he has been trained for so many years and has become nothing more than a cog in the organization of labor discipline, a proposition that cannot fail to be disturbing to at least some members of the profession.

The Soviet doctor, faced with a host of problems and decisions that bear little relation to traditional medical practice, finds it difficult to steer a course between compassion and indifference and may acquire a sense of hopelessness as evidenced in the outcry of the Ukrainian doctor quoted above[28]:

> . . .Sometimes we got together after work and asked ourselves: "What good are we doing to the people?" We just sat there and decided which one would we give a dispensation and which one we would not. . .Of course we helped some. . .but morally it was great suffering.

Causes of Soviet Malingering

The word "malingering" is used here to denote both the simulation of illness or injury and the requests for medical care on nonmedical ground described above. Generally speaking, physicians have paid scant attention to the social circumstances surrounding the presence of malingering, although they have been quick to detect that it was, in some respect, a cultural phenomenon, "a deplorable tradition" transmitted from person to person in certain classes or types. For example, a French doctor, writ-

ing on self-mutilations, mentions a list of 13 methods of malingering taken from a prisoner.[28] There is little doubt that military hospitals and prisons are fertile grounds for malingering knowledge, which in wartime attains the rank of a science. Physicians have, at times, suspected that there were special courses given on the subject.[29] As a matter of fact, in World War II, Germans dropped propaganda leaflets on British troops, entitled "Better a few weeks ill than all your life dead," which contained a complete set of instructions in simulation.[30] In this country the *Infantry Journal* made a reference to courses in psychoneurosis guaranteed to obtain either a rejection or a discharge from the Army,[31] and druggists were arrested for selling "goof balls" also known as "4-F pills" to cause rejection from Selective Service on "nervous grounds."[32] Physicians who have dealt with the subject have been prone to attribute it to dishonesty, lack of courage, sloth and desire for gain. They have also noticed that malingering was most prevalent in military and industrial life, where *monotony, danger, alienation* and *low remuneration* were prevalent.

To return to the Soviet situation, Soviet physicians interviewed suggested the hypothesis that two complementary elements accounted for the high rate of malingering. The first was the result of the decision taken in the early 1930's by the Soviet leaders to industrialize their country under forced draft without borrowing capital from abroad and without an adequately trained and disciplined labor force. This in turn led to a drastic *decrease in the standard of living* of the masses of the Russian population. The inability of the regime to provide adequate motivation for faithful and accurate work and the ever increased tempo of industrialization necessitated the imposition of ever *stricter discipline and regulations in all spheres of Soviet life* and particularly in production. For example, a series of decrees first introduced in the early 1930's tightened regulations on absenteeism and tardiness so that, by 1940, tardiness, of more than twenty minutes or repeated cases of minor tardiness, unless for a justifiable reason, became legal offenses punishable by a court sentence of compulsory labor without confinement at the usual place of employment for a maximum period of six months with a maximum wage deduction of 25 per cent. In view of the generally low standard of living of the greater part of the Soviet masses, the application of such regulations often results in undeserved and sometimes unbearable hardships for the "guilty" parties, who find themselves accused of "crimes" that they never intended to commit or committed through no fault of their own (for example, through a breakdown of the transportation system). At the same time a low standard of living, coupled with certain fixed expenses, means that a wage cut will affect the food budget. (According to figures recently obtained and valid for 1948, a man supporting a wife and two children would see his food budget cut by 38 per cent as a result of a 25 per cent wage cut; recent evidence, however, points to a definite increase in the standard of living.[33]) It is natural that the physician should be looked upon as the logical person to see in case of trouble. It may be assumed that as long as the social and economic situation remains the same, there will be a consistently high demand for medical certificates and that this demand per se is relatively independent of the fact that medical services are "socialized."

Resulting State Pressure upon the Physician

It stands to reason that a large-scale exploitation of the medical system would lead to a short-circuiting of social controls, and the "business" of the society would not get done. There are, then, certain "mechanisms" that to some extent cope with this problem. First of all, it may be assumed that the physician may well believe that if his attitude were too permissive the system would collapse. Sir John Collie[34] spelled out this principle more than 30 years ago when he wrote: "Surely it is the duty of the medical man to help the State count amongst her citizens the maximum number of units capable to work." Secondly, the doctor, as a professional, does not like the idea of being deceived by clever malingerers or sob-story spinners. Thirdly, he may believe that, pressures upon everyone, including himself, being fairly heavy, there is no justification for "undeserving" persons to exploit the medical system. Fourthly, the physician realizes that malingerers deprive the genuinely sick person of medical attention. Fifthly, there is the fear of *agents provocateurs* who request a sick-certificate and then report the physician to the authorities. As one doctor[35] said; "The physician is afraid, like everybody else. . .every patient could be an agent, the crying woman may be one, who knows?"

There is, in addition, a set of pressures applied directly upon the doctor. He is sensitive to these pressures because he is, in the majority of cases, a direct employee of the state, working for a salary and subject to the orders of the Ministry of Health and of its local organs. At the same time the physicians, like any other social and occupational group, are not allowed to organize themselves into independent professional associations that would enable them to take a stand against the encroachments of the state. Physicians may join the Union of Medical Workers (Medsantrud), which embraces everyone working in the field of health, including doctors, *feldshers* (doctors' assistants), nurses, attendants and cooks, and within this union, the physicians' sections. But these sections cannot in any respect be likened to local chapters of a national medical association.

The discretion of the physician is restricted by two conditions. In the first place, patients who claim

that they are sick must show a temperature above a certain minimum. This minimum fluctuates with the necessities of production and the urgency of the situation. Although temperature is not always a valid criterion for the diagnosis of illness and can easily be artificially produced, this condition definitely restricts the power of the physician. It is, of course, also possible for the physician to indicate in his record a temperature higher than the one observed, but even this small area of discretion is often narrowed down by the practice of having, in most cases, the nurse take and record the temperature herself. Under those circumstances the physician is reluctant to engage in forgery, since this would involve a third party and the possibility of a denunciation.

The second control mechanism (less generally used) consists in the issuance of definite and limited norms of sickness certificates to be granted in any one period. These norms, which can also be revised according to the situation, usually consist of a percentage of the number of persons on the physician's panel. The doctor who consistently exceeds his norms will be called upon to explain his actions, and may be threatened with sanctions unless he observes the quotas. A Soviet-trained physician, who was also chief of clinic and thus directly responsible for the work of his colleagues under him, said that he asked doctors who had gone over the norms: "How come, doctor, last week you delivered 15 certificates, and this week 17? And the doctor had to explain and prove — in other words to justify — his actions."[36] Another doctor reported that after exceeding his norm, he had been threatened with being accused of sabotage and hostility to the Soviet regime.[37] In the Soviet Union such an accusation is not to be taken lightly, since loyalty to the regime is the primary basis of personal security. There are, in addition, special commissions that check on the work of physicians, particularly in the spending of funds for social insurance and in areas of lagging productions.[38-40]

These control mechanisms make the performance of medical work difficult, and sometimes even dangerous. At the same time it might be easy to infer that under these circumstances the physician can well afford to disregard the interests of his patients by obeying all the orders he receives and thus playing it safe. This assumption is not, however, borne out by the evidence. There, again, other mechanisms force the physician to be concerned with the welfare of the persons he sees.

Pressures of the Patients and the State against the Physician

In spite of the manifold elements that interfere with the work of the Soviet physician, his primary function and *raison d'être* remain the maintenance of an adequate level of health among the population, on the assumption that illness and injury reduce production. In the scheme of Soviet production the doctor has his place as a preventive maintenance and repair engineer dealing with the human cogs of the industrial machine. The proposition is simple: "Sick or injured workers do not produce." It thus behooves the physician to lessen, so far as possible, the impact of illness upon society. The first mechanism may be said to be inherent in the nature of medical work itself and in the desire of the physician to perform his work by helping individuals. As one Soviet-trained doctor[41] declared:

> ...In principle the doctor must not behave as a technician working for financial rewards, but exclusively from the medical viewpoint...the very low pay that he received made it so that there was no financial motivation attached to the job of physician...most of them were idealists.

Or as another Soviet physician[42] put it: "Our work was our inner emigration." It is also relatively easy for the average physician to identify himself with the majority of his patients since his standard of living does not differ significantly from that of the Soviet masses.

There are, in addition, a set of formal pressures originating with the Ministry of Health, which is vitally interested in the good performance of its physicians and in the downward trend of time lost through illness; it thus urges the physician to prevent and detect illness that might become serious. Another source of pressure is the Soviet population itself in the following manner. The regime, in its propaganda, claims that, among other blessings, everything is done for the welfare of the population. Socialized medicine is presented as still another brilliant achievement of the Soviet system that could not be duplicated in capitalistic countries:

> The Soviet Union is the first country where the principle of free and socialized medical-sanitary assistance for everyone is realized. This is one of the many manifestations of the Stalinist concern for the individual...all the efforts of medical science are used in our country to protect the health of the workers...In the capitalistic countries medical assistance is available only to the rich...this is what happens when the working man does not count...where all is done for profits.[43]

It is also clear that these statements do not always correspond to reality and that medical care often falls short of expectations. In addition to the difficulties cited above, Soviet medicine is plagued with shortages of medical equipment, drugs and facilities, the poor quality of instruments, the bureaucratic procurement system and the lack of co-operation shown by local authorities and enterprises.[44-47] Soviet citizens are told that the deficiencies are faults of execution and not of design and are the result of bureaucratic apathy; they are then encouraged to report all such shortcomings. These reports usually take the form of critical letters to editors of newspapers, and are known as "Bolshevik self-criticism."[48,49] These letters, an example of which is

given above,[15] permit the release of aggression upon suitable targets and thus deflect it from the regime. The physician *is in no way immune from such criticisms,* which are, in the words of one of the physicians interviewed, a constant source of anxiety. As *Trud* [*Labor*] stated in an editorial; "Each fact of inattentive attitude to the patient, each case of insolence and irresponsibility, must become the subject of a social investigation and action."[50]

It may be assumed, then, that, regardless of the motives that may have urged (or even forced) the physician to behave in a certain manner toward patients (and Soviet conditions as described above are prone to produce endless irritations and frustrations) he will not relish seeing himself attacked or accused of negligence by laymen, particularly since these accusations may have dire consequences in the form of drastic punishment. Again, the letter[15] mentioned above states:

> Of course, one cannot demand that in every case the doctor make a faultless diagnosis. Mistakes are possible but that is not here or there. What is completely intolerable is that a physician who cannot determine the nature of an illness should insult his patient. This is precisely the way doctor Cherkessova and Professor Voronov behaved toward their patients. They call this being heartless. Is that all?

In the same issue of *The Medical Worker* it is reported[15] that readers wrote about the inattentiveness of a certain doctor in a district clinic:

> A check-up by the Volynsky Regional Health Department confirmed the reported situation and Doctor Portnoy was removed. Also, Comrade Leontiev head of the Manevichsky District Health Department received an administrative reprimand for lack of supervision of clinic work.

The Ministry of Health and its lower echelons also maintain specially designated bureaus, which deal with the investigation and appropriate action to be taken in these cases. Another article in *The Medical Worker,*[51] for example, reports on the work of these bureaus and notices "some improvement in the examination of complaints and statements of workers." In some cases the State arranges "show trials" to demonstrate its concern with the "health of the toilers"; in these trials the doctor may be prejudged guilty regardless of the medical merits of the case. In this respect the lack of a strong professional organization prevents other physicians from helping their colleagues, particularly when these colleagues are considered as "enemies of the people." To testify in their favor would mean siding against "the people." In this respect, it is significant that in the fantastic accusations of "medical murder" leveled at nine prominent Soviet doctors in mid-January, 1953, no physician or body of physicians demanded an impartial investigation of the charges. Rather, one physician, Lydia F. Timachuk, was awarded the Order of Lenin for the assistance she gave the government in "unmasking the doctor-murderers."[52] (When subsequently the doctors were released on the grounds that the accusations had been fabricated, their jailers were in turn sent to prison; Dr. Timachuk also lost her order.)

The Soviet physician finds himself in an anomalous situation. Trained and urged to behave "like a doctor," he is often prevented from doing so, and must often pay for this failure. There appears to be enough evidence in official Soviet sources to prove that this situation is not unique with the doctors who were interviewed, but is part of medical practice under Soviet conditions.

Discussion

The difficulties experienced by the Soviet physician are the result of factors present both in the Soviet situation and in a system of socialized medicine. Undoubtedly, a low standard of living, coercive measures and totalitarian controls, as well as the low priority accorded the life and health of the worker (except as a producing instrument), exacerbate rather than mitigate certain inherent defects of socialized medicine such as excessive bureaucratization and unwarranted layman interference in professional matters. (At the same time, it must be recognized that whereas it is true that medicine has become one of the links in the Soviet system of controls, to claim that state-supported medicine in other societies would bring a Soviet regime is tantamount to saying that the Army Medical Corps makes casualties unavoidable.) It may be supposed, in addition, that if the fundamental ideologic and political commitments of the Soviet leaders moved toward a more humanitarian form, this change would be reflected in better medical care for the population and easier working conditions for the physician. Indeed, the Displaced Persons as a whole, and most of the interviewed physicians, considered the design (if not the execution) of socialized medicine as one of the most positive elements in the Soviet scheme (ranking second only to popular education) and one they would like to retain and improve upon if a change of regime were feasible. There is, furthermore, reason to believe that under certain specific types of social organization, some form of "socialized medicine" is the only solution to the problem of medical care. (It would, for example, be difficult to conceive of private medical practice in the armed forces.)

It may finally be argued that strain in the role of the Soviet doctor reflects, to some extent, a degree of social malintegration and malaise but that the physician cushions or softens the impact of the regime upon the individual. Thus, from the point of view of the society as a functioning system, the work of the physician may be seen as one of the many "adjustive mechanisms" that keep the social organism going by limiting discontent and hence disaffection. Although this role is undoubtedly hard on the doctor, he appears to realize the positive functions

he performs and apparently derives some satisfaction from it. As one physician, employed in a concentration camp, declared to Elinor Lipper, who was at that time an inmate: "Camps are made to tighten the screws on the prisoners, and we physicians are here to loosen them a bit."[53] With some modification, this applies to the work of the Soviet doctor in general.

Summary

Besides his medical functions, the physician delivers socially recognized excuses from normal obligations and sanctions.

In Soviet society, for a variety of reasons noted, attempts are made to manipulate these excuses for nonmedical purposes. The Soviet State consequently applies pressure on the physician to reduce this manipulation and to ensure the highest industrial and agricultural productivity by its citizens.

Although malingering is a sign of social disorganization, the physician by mitigating the impact of the regime on his patient is a source of stability and integration.

The excesses of malingering in Russia appear primarily to be due to coercive work measures and a considerable disregard for the individual's welfare. They are not directly related to the organization of Soviet medicine.

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PANCREATICODUODENAL CANCER

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THE term pancreaticoduodenal cancer was introduced by Child[1] to characterize a group of malignant tumors that arise in the region of the ampulla of Vater. It therefore includes tumors of the head of the pancreas, the ampulla of Vater, the common bile duct and the duodenum. All these cancers have in common the fact that a relatively standardized operation, pancreaticoduodenectomy, has been employed in their removal. Carcinomas of the body and tail of the pancreas present a different technical problem and have therefore been excluded from the present study.

Since Whipple and his associates[2] described a method of surgical approach to these tumors in 1935, a number of authors[1, 3-8] have attempted to appraise the results of radical surgery. Despite Clifton's[9] optimistic report and isolated records of five-year survivals,[9-11] the consensus has been that the operation as performed has been relatively ineffective for carcinoma of the head of the pancreas. More optimism has been expressed about surgical removal of cancer of the ampulla of Vater, the common bile duct and the duodenum. This impression may be inaccurate because no effort has been made to compare the results of radical surgery with the course of patients treated in the years before radical resections were done. The object of this study is to present the results of radical resection of pancreaticoduodenal carcinoma at the Massachusetts General Hospital and to compare the postoperative survival of these patients with that of patients on whom only palliative procedures were performed.

The first pancreaticoduodenectomy at the Massachusetts General Hospital was performed in 1941. It is reasonable to compare the results of surgery, both "curative" and palliative, during the last ten years (1941–1950) with the clinical course of the same types of carcinoma during the preceding decade (1931–1940), during which only palliative surgery‡ was employed regardless of the size of the tumor, duration of symptoms or condition of the patient. The comparison between these two groups of cases should give a reasonable picture of what radical surgery has accomplished. The comparison of the resections alone with any other group gives a distorted picture because the resected cases are obviously selected. The fact that no radical resections were undertaken before 1941 excludes selection of patients. Because the present study is directed toward the evaluation of long-term results, survival figures have been computed only on patients who left the hospital alive.

There were 132 patients with pancreaticoduodenal cancer admitted to the Massachusetts General Hospital from January 1, 1931, through December 31, 1940, and 183 during the decade January 1, 1941, through December 31, 1950. Eight cases during the entire twenty-year period were lost to follow-up study and have not been included in the series; none of these, however, were in the resected group. The over-all resectability rate and the hospital mortality attendant on pancreaticoduodenectomy is shown in Table 1. For purposes of evaluation the entire group of cases has been broken down into the four categories mentioned in Table 2. Each is given separate consideration.

TABLE 1. *Resectability and Mortality in Pancreaticoduodenal Cancer, 1941–1950.*

	No. of Cases	%
Total	183	
Resected	65	35
Hospital mortality	22	34

TABLE 2. *Types of Pancreaticoduodenal Cancer, 1931–1950.*

Type of Case	No. of Cases 1931–40	No. of Cases 1941–50
Cancer of head of pancreas	112	136
Cancer of ampulla of Vater	9	24
Cancer of common bile duct	10	17
Cancer of duodenum	1	6
Totals	132	183

CANCER OF THE HEAD OF THE PANCREAS

Cancer of the head of the pancreas has generally been recognized as being associated with the shortest survival of the entire group of pancreaticoduodenal carcinomas. It is therefore not surprising to find that the average duration of life after pancreaticoduodenectomy was only eleven months. This figure coincides reasonably well with the average survival of thirteen months reported by Loggan and Kleinsasser[8] in their collective review of all the pancreaticoduodenal resections for cancer of the head of the pancreas reported in the literature. Discouraging as this figure is, it is even more disheartening to find that the average survival of the resected and

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‡The term palliative surgery as used in this report refers to any one of several types of operations (cholecystogastrostomy, cholecystenterostomy, choledochoenterostomy and so forth) designed to by-pass the obstruction to the flow of bile into the gastrointestinal tract.

palliated cases was slightly less than that of a comparable group during the preceding decade when no radical resections were done (Table 3). There has been no increase in average survival since the addition of radical surgery to previously employed palliative procedures. This suggests that the longer survival in the cases of resection, as compared with disease, after forty-eight months. With this perspective of pancreaticoduodenectomy for cancer of the head of the pancreas, it is fair to say that 2 patients out of the entire group were benefited by resection. The value of radical surgery is always difficult to assess because of the many factors involved, but it is only fair to point out that the hos-

TABLE 3. *Survival among Patients with Carcinoma of the Head of the Pancreas.*

PERIOD	METHOD OF TREATMENT	NO. OF CASES	DEATHS IN HOSPITAL		PATIENTS WHO SURVIVED	AVERAGE DURATION OF LIFE OF SURVIVORS	
			NO.	PERCENTAGE			mo.
Jan. 1, 1931, through Dec. 31, 1940	No operation or exploratory laparotomy	37	15	40	22	2.0	7.7
	Palliative procedure	75	29	39	46	7.7	
	Resection	0	0	0	0	0	
Jan. 1, 1941, through Dec. 31, 1950	No operation or exploratory laparotomy	36	22	61	14	2.0	6.2
	Palliative procedure	67	16	24	51	4.0	
	Resection	33	10	30	23	11.0	

that in cases of palliative procedures only, may be attributed to the selection of patients with more favorable tumors for radical surgery.

Since the average survival may give a false impression of any cancer therapy, percentage survival

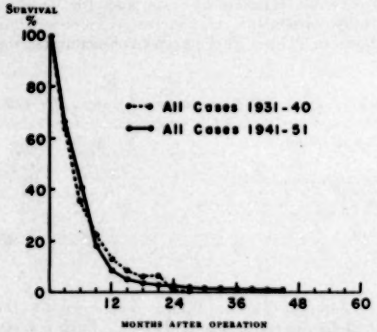

FIGURE 1. *Survival among Patients with Carcinoma of the Pancreas Who Left the Hospital Alive.*

by three-month periods has been calculated for all patients who left the hospital alive with a diagnosis of cancer of the head of the pancreas (Fig. 1 and 2). If one compares the percentage survival curve of all cases from 1931–1940 with that of all cases from 1941–1950 (the "resection for cure" era), it is apparent that up to twenty-seven months, the curves are nearly identical (Fig. 1). Beyond this point all patients whose cancers were not resected were dead, whereas 2 patients who underwent pancreaticoduodenectomy were still alive. One died of recurrent disease thirty months after leaving the hospital; the other is still alive, without evidence of pital mortality after resection in this group has been 30 per cent, and this must be considered when reference is made to the 2 patients whose lives were apparently extended by resection.

CARCINOMA OF THE AMPULLA OF VATER

The figures shown in Table 4 bear out the impression that carcinomas of the ampulla of Vater carry a more favorable prognosis than those originating in the head of the pancreas. Whether this can be attributed to the biologic characteristics of the tumor itself or whether the site of origin at the

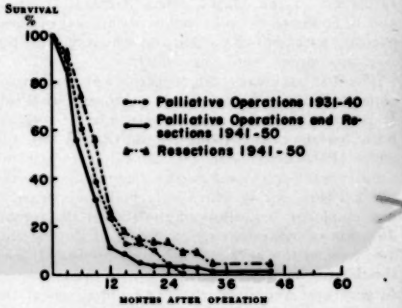

FIGURE 2. *Survival, According to Type of Operation Performed, among Patients Who Left the Hospital Alive.*

opening of the bile duct results in earlier clinical recognition of the disease is beyond the scope of this report. The interesting fact derived from these figures is that the average survival in carcinoma of the ampulla of Vater has not been altered appreciably by the introduction of resection for cure although in this series, as in other reports, there were

a few long survivals after resection. One patient lived over five years and another four years after resection. Both died of recurrent disease. None of the patients with cancer of the ampulla of Vater are still alive at present.

Because of the relatively small number of cases no attempt has been made to plot survival curves. From these figures, however, and from the individual consideration given to long-term survivals in Table 7, it is possible to say that "resection for cure" may have extended the survival of a few patients and may achieve isolated five-year cures. Certainly, it has not yet accomplished the results for which one might have hoped.

TABLE 4. *Survival among Patients with Carcinoma of the Ampulla of Vater.*

PERIOD	METHOD OF TREATMENT	NO. OF CASES	DEATHS IN HOSPITAL		PATIENTS WHO SURVIVED	AVERAGE DURATION OF LIFE OF SURVIVORS	
			NO.	PERCENTAGE			
						mo.	
Jan. 1, 1931, through Dec. 31, 1940	No operation or exploratory laparotomy	0	0	—	0	—	21.0
	Palliative procedure	9	4	44	5	21.0	
	Resection	0	0	—	0	0	
Jan. 1, 1941, through Dec. 31, 1950	No operation or exploratory laparotomy	2	2	100	0	—	18.5
	Palliative procedure	4	1	25	3	7.5	
	Resection	18	5	28	13	21.0	

TABLE 5. *Survival among Patients with Carcinoma of the Common Bile Duct.*

PERIOD	METHOD OF TREATMENT	NO. OF CASES	DEATHS IN HOSPITAL		PATIENTS WHO SURVIVED	AVERAGE DURATION OF LIFE OF SURVIVORS	
			NO.	PERCENTAGE			
						mo.	
Jan. 1, 1931, through Dec. 31, 1940	No operation or exploratory laparotomy	5	3	60	2	4.0	6
	Palliative procedure	4	1	25	3	3.0	
	Resection	1	0	—	1	15.0	
Jan. 1, 1941, through Dec. 31, 1950	No operation or exploratory laparotomy	2	1	50	1	7.0	12.7
	Palliative procedure	7	1	14	6	5.6	
	Resection	8	5	71	3	27.0	

TABLE 6. *Survival among Patients with Carcinoma of the Duodenum.*

PERIOD	METHOD OF TREATMENT	NO. OF CASES	DEATHS IN HOSPITAL		PATIENTS WHO SURVIVED	AVERAGE DURATION OF LIFE OF SURVIVORS	
			NO.	PERCENTAGE			
						mo.	
Jan. 1, 1931, through Dec. 31, 1940	No operation or exploratory laparotomy	0	0	—	0	—	36
	Palliative procedure	1	0	—	1	36	
	Resection	0	0	—	0	—	
Jan. 1, 1941, through Dec. 31, 1950	No operation or exploratory laparotomy	0	0	—	0	—	35
	Palliative procedure	0	0	—	0	0	
	Resection	6	2	33	4	35	

CARCINOMA OF THE COMMON BILE DUCT

The relative infrequency of carcinoma of the common bile duct could easily make statistics misleading. Nevertheless, it appears that, like the tumor of the ampulla of Vater, carcinoma of the common bile duct carries a more favorable prognosis than carcinoma of the head of the pancreas (Table 5), but the average survival has not been increased greatly by the addition of resection. The comments made on carcinoma of the ampulla of Vater are applicable to this group as well. It should be made clear that carcinomas of the gall bladder, common hepatic duct and biliary radicles are not included, for the anatomic location of these structures is such that they do not properly belong under the heading of pancreaticoduodenal tumors.

CARCINOMA OF THE DUODENUM

There is a widespread impression that carcinomas of the duodenum are highly malignant lesions. For that reason the figures in Table 6 were of particular

interest. Obviously, statistical analysis is impossible because of the rarity of this tumor and the small number of cases in this series. The fact that all 6 patients in whom the diagnosis was established between 1941 and 1950 had resectable lesions and that, of these, 2 may well be cured makes it hard to escape the conclusion that these tumors carry a prognosis at least as good as if not better than that of any lesion in this series. All the histologic sections were not available for re-examination, but several of these tumors, some of which at least may arise from Brunner's glands, appeared to be of low-grade malignancy.

TABLE 7. *Patients with Pancreaticoduodenal Cancer Surviving Resection for More Than Eighteen Months (1941–1950).*

PATIENT	M.G.H. No.	AGE	SEX	LOCATION OF LESION	DATE OF OPERATION	POST-OPERATIVE SURVIVAL	COMMENT
		yr.				mo.	
A. Y.	314697	59	M	Ampulla of Vater	1941	64	Patient died with liver metastases
B. W.	448260	61	M	Head of pancreas	1944	24	Patient died with recurrent disease
C. R.	295218	53	F	Head of pancreas	1946	19	Patient died with recurrent disease
V. P.	555370	53	M	Duodenum	1946	66	Patient living and well
F. B.	583922	75	F	Head of pancreas	1947	30	Patient died of recurrent disease
A. B.	610976	58	F	Duodenum	1948	49	Patient living and well
W. M.	605959	62	M	Common bile duct	1948	52	Patient living and well
S. N.	552386	55	M	Head of pancreas	1948	48	Patient living and well; reoperation for jejunal ulcer 45 mo. after resection.
A. R.	160314	68	F	Ampulla of Vater	1948	48	Patient died of liver metastases; two subsequent palliative procedures done because of recurrent obstructive jaundice.
V. M.	586814	62	F	Ampulla of Vater	1948	19	Patient died of recurrent disease
E. S.	654944	38	M	Ampulla of Vater	1949	32	Patient died of recurrent disease
E. P.	567635	47	M	Ampulla of Vater	1949	19	Patient died of recurrent disease
A. B.	669773	49	M	Duodenum	1949	23	Patient died of recurrent disease
D. R.	722320	73	M	Common bile duct	1950	18	Patient living and asymptomatic although biliary obstruction from recurrent cancer necessitated a palliative operation 1 yr. after primary resection.

DISCUSSION

The results of this study were naturally disheartening because it must be admitted that little or nothing has been accomplished in this group of tumors from the point of view of over-all salvage. An analysis of any series of resections might not bring out this failure so conspicuously unless a comparable group of cases from the era before any resections were done was concomitantly analyzed and studied. Nevertheless, although statistics may be valuable in affording an objective panorama of results and in delineating clearly the over-all success or failure of a method of therapy, it is essential to realize that statistics do not of necessity apply to an individual patient. For this reason, we have recorded in Table 7 the status of all patients in this series who have survived more than eighteen months after pancreaticoduodenectomy. These results indicate that in some cases radical resection has been of palliative value and, in a still smaller group, has achieved five-year survival and possibly permanent eradication of the disease. Therefore, even on the basis of these discouraging statistics, one should not advocate abandonment of pancreaticoduodenectomy even in cancer of the head of the pancreas, which has the most unfavorable prognosis of the entire group.

There are many possible reasons that could be offered to account for these poor results, but the one most amenable to direct attack is the technic of pancreaticoduodenectomy as it is carried out at present. Any resection for cancer that leaves behind the main venous and lymphatic channels draining the anatomic site of origin of the cancer (in this case, the portal vein and tributaries, and the lymphatics of the gastrohepatic ligament) will obviously fail except in a few isolated cases. For this reason one of us[12] and Child et al.[13] have independently reported a method of pancreaticoduodenectomy that includes resection of the portal vein and the accompanying lymphatic system. It will be many years before it will be possible to assess the results of this extension of an already formidable surgical operation. If the physiologic effects of the interruption or shunting of the portal circulation prove unsatisfactory, or if no improvement is apparent in the over-all salvage, consideration should be given to the possibility of abandoning all attempts at radical resection of any but the most favorable of these tumors.

SUMMARY AND CONCLUSIONS

The results of pancreaticoduodenectomy for cancer of the head of the pancreas, ampulla of Vater, common bile duct and duodenum over a ten-year period are analyzed and compared with those in a similar group treated by palliative surgery during the preceding decade when no resections were attempted.

The inevitable conclusion to be drawn from a comparison of these two groups is that little or nothing has been accomplished by pancreaticoduo-

denectomy if the results are viewed from the point of view of over-all salvage. Nevertheless, isolated patients in this and other series have obviously been benefited by radical surgery, particularly in cancer of the duodenum, which, in a small series, seems to carry a relatively favorable prognosis.

Recently described methods of resection of the portal vein and accompanying lymphatics may prove to be of value in improving the results of radical surgical removal of these tumors.

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TREATMENT OF RESPIRATORY ACIDOSIS WITH N-ALLYLNORMORPHINE (NALLINE)*

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In 1943 Unna[1] first reported the results of animal studies on the antagonistic properties of N-allylnormorphine (Nalline) to morphine. In recent years, the therapeutic application of these properties has been under investigation in human subjects.[2-4]

Nalline is chemically related to morphine by the substitution of an allyl bromide group in the morphine radical.[1, 5] It counteracts the toxic effects of morphine in animals, especially the depression of respiration, and in some animals it apparently serves as a mild analgesic drug.[1] In human beings it not only has no demonstrable analgesic activity in itself but also abolishes the analgesic effects of morphine and its derivatives.[3] The important action of Nalline seems to lie in counteracting the respiratory depression induced by synthetic or natural opiate alkaloids.[3,6] Among the respiratory-depressant drugs that have been successfully counteracted by Nalline are morphine, Pantopon, Dilaudid, Demerol, Methadon, Metopon, Dromoran and codeine; those not favorably counteracted have been ether, barbiturates and cyclopropane.[3]

Certain other effects of this drug have been recorded in the literature. In animals[1] Nalline reduces the blood pressure, whereas in human beings[2] it is reported to have increased the blood pressure. The effect on the pulse rate has been variable. Some opiate-induced metabolic disturbances, such as hyperglycemia, are effectively counteracted if the drug is administered before the opiate is given.[7, 8] The action on reflexes, according to Carter,[9] appears to be one of hyperactivity. It has also been reported in the literature that this drug is a true cholinesterase inhibitor, and it has been found to be more potent than morphine in this regard.[10]

Clinical Results

The purpose of this paper is to report the successful clinical use of Nalline in 4 cases of respiratory acidosis resulting from overdosage of opiates or barbiturates. Laboratory data accompanying the first 2 cases demonstrate the correction of the respiratory acidosis (morphine induced) and restoration to normal. The other 2 patients, who were successfully treated for respiratory depression induced by barbiturates (Pentothal and Surital) represent, we believe, the first cases in which the favorable action of Nalline in barbiturate intoxication has been reported. Our observations in these patients led us to discuss a possible mechanism of action of Nalline.

Case Reports

Case 1. L. D., a 78-year-old woman, was admitted to the hospital at 11 a.m. in a comatose state, the respiratory rate being 3 per minute. There was evidence of marked miosis and cyanosis. An incarcerated right inguinal hernia had suddenly developed 36 hours previously, and 2 hours before admission, her physician had subcutaneously administered 30 mg. (½ gr.) of morphine. Shortly thereafter she became progressively comatose. We saw the patient for the first time at 1 p.m. After the control values listed in Figure 1 had been obtained 5 mg. of Nalline was given

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intravenously by slow drip (1 minute) at 1:15 p.m. The sequence of events is illustrated in Figure 1. The respiratory acidosis indicated by the initial (control) drop in pH and abnormally increased pCO_2 (arterial carbon dioxide tension) were corrected promptly upon adequate restoration of the patient's minute ventilation, the effects being noted within 2 minutes of administration of the drug. The acid-base balance returned to normal in 77 minutes after a total dose of 25 mg. On the following day the patient was successfully operated on for the hernia, and she recovered uneventfully.

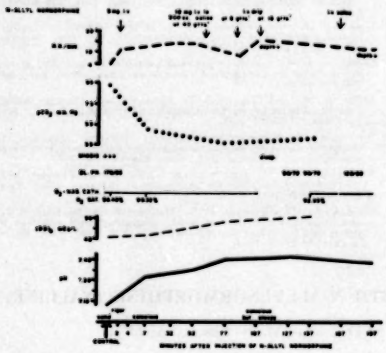

FIGURE 1. *Treatment of Respiratory Acidosis (Morphine Induced) with Nalline (Reproduced from Segal and Dulfano,[11] with the Permission of the Publishers).*

By changing the rate of the intravenous infusion drip in administering the total dose of 25 mg. of Nalline over a period of seventy-seven minutes, we were able to obtain immediate, striking changes in the respiratory rate and depth. These changes were interpreted as the result of a direct, stimulating effect of the drug on the respiratory center.

CASE 2. C. M., a 79-year-old man, entered the hospital complaining of substernal pain. He had had angina pectoris for the past 12 years and was being treated with maintenance doses of nitroglycerin, 0.6 mg. (1/100 gr.) 3 times a day.

Twelve hours before admission he experienced severe substernal pain, which was not relieved by 0.6 mg. of nitroglycerin. At 8 a.m. his physician administered 15 mg. (¼ gr.) of morphine sulfate. This brought no relief and at 8:45 a.m., 10 mg. (1/6 gr.) of morphine sulfate was given. Because pain persisted, he was admitted to the hospital, where he received an additional 10 mg. of morphine sulfate, making a total of 35 mg. within a period of 3 hours. At 1:30 p.m., still in distress, he received 75 mg. of Demerol intravenously. At 2 p.m. the respiratory rate had dropped to 7 per minute, from the admission rate of 18 per minute. At 2:30, when he was seen by one of us, he appeared semicomatose: the pupils were miotic, and the deep tendon reflexes sluggish, the pulse was 108 beats per minute, and the blood pressure was 120/80 (Table 1). Oxygen by nasal catheter at a flow of 6 liters per minute was administered. He appeared cyanotic; respiration was extremely shallow, and the heart sounds were distant. After an arterial blood sample had been drawn (control values) for laboratory study, 10 mg. of Nalline was administered intravenously at 2:50 p.m. Within 5 minutes, the respiratory rate increased to 17 per minute, the pulse rate remained the same, the blood pressure increased to 135/80, the pupils were semi-dilated, and the deep tendon reflexes became hyperactive. The heart sounds and color improved progressively and by 3 p.m. the patient responded to questioning. Ten minutes after the administration of Nalline the respiratory acidosis was corrected (Table 1). He was fairly alert by 3:10, when the blood pressure had increased to 140/80 and the respirations to 26 per minute. At 3:20, because the respiratory rate had dropped to 17 per minute, he was given an additional dose of 30 mg. of Nalline in 200 cc. of 5 per cent glucose in water over a period of 15 minutes, but there was no further demonstrable change in his clinical condition. Additional arterial blood samples were obtained (Table 1).

TABLE 1. *Effect of Nalline on Morphine-Induced Respiratory Acidosis in Case 2.*

TIME OF DETERMINATION	ARTERIAL CARBON DIOXIDE TENSION	ARTERIAL CARBON DIOXIDE CONTENT	ARTERIAL BUFFER BASE	ARTERIAL OXYGEN SATURATION	ARTERIAL pH	RESPIRATORY RATE	DEPTH OF RESPIRATION	BLOOD PRESSURE	PULSE	OXYGEN FLOW	CENTRAL-NERVOUS-SYSTEM SYMPTOMS
	mm. Hg.	*millieqvis./liter*	*millieqvis./liter*	*%*		*per min.*			*per min.*	*liters/min.*	
On admission (control value)	52	23.60	48	92	7.32	7	Shallow	120/80	108	6	Patient semicomatose, with miosis and hyperreflexia
5 min. after 1st dose of Nalline*						17	Increased	135/80	108		Patient aroused, with semidilated pupils and hyperreflexia
10 min. after 1st dose of Nalline	42	23.70	53	94	7.42	24		140/104	108		
20 min. after 1st dose of Nalline						26		140/80			Patient responsive, with normal reflexes
30 min. after 1st dose of Nalline†						17		140/80			
45 min. after 1st dose of Nalline					7.33	24	Shallow	144/100	108		Patient sleepy
60 min. after 1st dose of Nalline	44	21.15	49	93	7.35	22	Shallow	140/96	108		Patient responsive

*10 mg. of Nalline, given intravenously at 2:50 p.m.

†2d dose (30 mg. of Nalline in 200 cc. of glucose solution) given intravenously at 3:20 p.m.

Rapid and sustained effects were obtained with a single dose of 10 mg. of Nalline given intra-

venously. No further improvement was noted from a second intravenous dose.

CASE 3. J. H., a healthy 41-year-old man, was given 1.5 gm. of Pentothal, 2 per cent solution, during extraction of all his teeth. No other premedication was given. The total operating time was 1 hour. Immediately after the operation the respirations were noted to be shallow, at a rate of 8 per minute. The pulse rate was 90, and the blood pressure 80/60; the color was good, and the pupils were miotic. The patient was sleeping and did not respond to questioning. At 11:15 a.m., 2 hours after the end of the operation, he was given 20 mg. of Nalline intravenously. At 11:20, the blood pressure increased to 100/80, the respiratory rate to 16, with increased depth, and the pulse rate to 90, and the deep tendon reflexes became more active. At 11:25 the blood pressure was 110/85; the respiratory rate decreased to 12 per minute and became more shallow, whereas the pulse rate remained at 90. At this point, however, the patient started to respond to questions, and the tendon reflexes became hyperactive. He was apparently waking up and began to move his arms and legs. At 11:40, because of the slow respiratory rate, he was given an additional dose of 20 mg. of Nalline intravenously. Within 5 minutes, the respiratory rate was again 16, the blood pressure and pulse remaining the same. The patient was able to sit up and responded to commands. Further recovery was complete and uneventful.

The successful response to Nalline therapy in a patient with respiratory depression induced by a barbiturate required 40 mg., a considerably higher dose than any previously employed in the management of opiate-induced respiratory depression.

CASE 4. M. D., a 48-year-old woman, received 2 gm. of Surital by intravenous drip with nitrous oxide anesthesia during a radical mastectomy that lasted 4¼ hours. No other premedication was given. At the end of the operation, although receiving oxygen at a flow of 6 liters per minute, she appeared cyanotic; the respiratory rate was 7 per minute and shallow, the blood pressure 80/60, and the pulse 100. She could not be roused by stimuli, but there was no evidence of shock. At 2 p.m., after the intravenous administration of 15 mg. of Nalline, the respiratory rate increased to 14 per minute, with increased depth. The blood pressure rose to 100/80, the pulse remaining unchanged, and there was no evidence of cyanosis. She was still receiving adequate oxygen concentrations but remained unresponsive to questioning and stimuli. At 2:15 her color again became cyanotic; the blood pressure stayed the same, but respirations were more shallow and decreased to 10 per minute. At this point an additional 20 mg. of Nalline was given intravenously. At 2:35 the respiratory rate increased to 17 per minute and became deeper, and the blood pressure rose to 120/80. The patient responded to supraorbital pressure and began moving her arms and legs, the deep tendon reflexes having become more active. At 2:45 the respiratory rate increased to 20 with normal depth; the blood pressure was 125/80, and the pulse rate 100, and the patient began to respond to questioning. Further recovery was uneventful.

A total dose of 35 mg. of Nalline administered in forty-five minutes was successful in reversing the depression caused by Surital intoxication.

DISCUSSION

In these 4 cases of respiratory depression, 2 caused by opiates (morphine and Demerol) and 2 by barbiturates (Pentothal and Surital), N-allylnormorphine (Nalline) was successful in restoring the respiration to normal. The laboratory data on the patients with opiate overdosage are shown in Figure 1 and Table 1.

Integration of our laboratory studies and clinical observations seem to point to the probable mechanism responsible for the action of Nalline. The confirmation of respiratory acidosis in both cases in which we were able to test the arterial blood suggests that the therapeutic scope of Nalline should be broadened.

Morphine and barbiturates specifically act as depressors of the respiratory center; the response of the respiratory center to carbon dioxide accumulations is highly diminished and respiratory acidosis ensues. This is the cause of death in many patients. It has been postulated that Nalline acts as an antidote to morphine by way of enzymatic destruction.[12] Our own observations indicate a different conception. Although a single dose of Nalline served to counteract certain toxic manifestations of morphine, repeated doses were necessary to overcome the symptoms of intoxication, which recurred after several minutes of improvement. Apparently, there could therefore not have been a parallel destruction of morphine by Nalline, but a stimulation of the central-nervous-system centers that temporarily counteracted or inhibited the toxic effects of morphine. This was particularly noticeable in the respiration: each dose of Nalline was followed by an immediate increase in the rate, and sometimes the depth, of respiration; and each change in rate of the Nalline drip also brought an immediate response. Such effects we interpreted as originating from a stimulus to the respiratory center. Pupillary changes, increased psychic responsiveness and orientation, and increased voluntary muscular activity suggest a direct stimulation of most of the central-nervous-system centers.

Our theory on the action of Nalline may be summarized as follows. It directly stimulates the central nervous system, especially the respiratory center, and thereby elevates the threshold of this center to depression by morphine. It appears also that the effects disappear promptly, since it is necessary to repeat the dose to maintain the improvement. Whether this is due to an accumulation of metabolites in the respiratory center similar to that occurring after the administration of caffeine or Coramine or to the presence of morphine that is still bound to the central nervous system, or to both, is not yet clear. The existence of a competitive displacement between Nalline and morphine in the enzyme-coenzyme systems affecting the central nervous system is another possibility.

Administration of Nalline by continuous infusion, after an effective single intravenous dose has been administered and maintained until a sustained response is obtained, seems to be the treatment of choice. This could also counteract the delayed release of morphine into the circulation from depots where it might be stored.

It is suggested that Nalline may be useful under circumstances presenting severe respiratory acidosis not related to drug intoxication. *It is particularly*

worth considering in acute and chronic pulmonary diseases.

Other investigators have reported that Nalline has been ineffective in the treatment of respiratory depression induced by barbiturates. Although our experience is limited, the results obtained in the 2 cases presented above encourage us to postulate that larger doses than those previously used in opiate intoxication may have the same good results. Further investigation is warranted.

Summary

Respiratory depression in 4 patients, induced in 2 by morphine and in 2 by barbiturates, was treated successfully with Nalline. The laboratory data on 2 cases showed the reversal of respiratory acidosis.

Several hypotheses concerning the action of Nalline are discussed. It is our impression that Nalline acts primarily as an analeptic drug, with a preferential action on the respiratory center.

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HYPERCALCEMIA OF SARCOID CORRECTED WITH CORTISONE*

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THE course of Boeck's sarcoid is characteristically said to be benign.[1] However, significant impairment of vital organs is not uncommon. Most frequently noted are eye involvement, which may lead to diminished vision or blindness,[2] and pulmonary lesions resulting in fibrosis of lung parenchyma, pulmonary insufficiency and cor pulmonale.[3]

A less emphasized abnormality in sarcoidosis is hypercalcemia and its attendant dangers to the patient. In the following case, reversal of hypercalcemia was accomplished with cortisone.

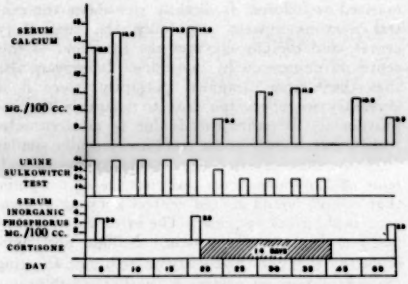

FIGURE 1. *Effect of Cortisone on Serum Calcium and Serum Inorganic Phosphorus.*

Case Report

A 28-year-old man had fever, migratory joint pain and red nodular lesions of the skin of the anterior surface of both legs in May, 1950. He was ill for 1 week, after which he was asymptomatic. An x-ray film of the chest showed a diffuse, fine stippling in both lung fields, without hilar lymphadenopathy. Films of the hands were normal, as were the serum albumin and globulin. A skin test with second-strength P. P. D. (purified protein derivative) was positive. Diagnoses of erythema nodosum and possible Boeck's sarcoid were made.

The patient was symptom free until April, 1952, when he noted anorexia, fatigue and a weight loss of 35 pounds over a period of several weeks. Skin lesions scattered on the upper extremities and trunk were also seen. Study at another institution was said to have shown impaired renal function. An intravenous pyelogram revealed no dye visible in the region of the kidney. Skin and sternal-marrow biopsies were not diagnostic. The patient was transferred to the Veterans Administration Hospital with a tentative diagnosis of sarcoid.

Physical examination demonstrated a well developed, thin man. The blood pressure was 120/70. There were several shot-size lymph nodes in the neck. The lungs were clear. The skin showed a number of erythematous, shiny papules on the upper extremities and trunk. The rest of the examination was not remarkable.

Examination of the blood disclosed a hemoglobin of 12.4 gm. per 100 cc. and a normal white-cell count. The blood Kahn reaction was negative. The thymol turbidity was 12 units. The blood sugar was 97 mg., the serum albumin 3.7 gm., and the globulin 2.5 gm. per 100 cc. The blood urea nitrogen was 11 mg. per 100 cc. The urine gave a + test for albumin, and the sediment contained 1 red cell, 4 white cells and an occasional hyaline cast per high-power field. The phenolsulfonephthalein test showed 7 per cent excretion of the dye in the first 15 minutes and a total of 28 per cent in 2 hours. A Fishberg concentration test revealed the highest specific gravity to be 1.014. The serum calcium was 14.4 mg., the serum inorganic phosphorus 3.4 mg., and the alkaline phos-

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phatase 4.3 Bodansky units per 100 cc. The Sulkowitch test for calcium in the urine was ++++.

An x-ray film of the chest revealed an increase in the stippling in both lung fields and also prominence of the hilar lymph nodes. Films of the hands were again normal.

Biopsy of the gastrocnemius muscle taken at random revealed a granuloma consistent with sarcoid, as did biopsy of a skin lesion of the thorax.

Further serum calcium determinations were consistently elevated, with a normal serum phosphorus (Fig. 1). A balance study showed a urinary excretion of 460 mg. of calcium per 24 hours on a diet containing 137 mg. of calcium.

The patient was given cortisone in a dosage of 300 mg. the 1st day and 200 mg. the 2d day and then 100 mg. for 12 days. By the 3d day of treatment the serum calcium had fallen to normal levels, where it remained. It is of note that the serum calcium remained within normal limits not only during the period of treatment but also after therapy with cortisone had been discontinued, during a six-month follow-up period. To date there has been no improvement in the specific gravity of the urine. The areas of density in the chest film did not change with therapy, but the skin lesions disappeared. A 24-hour excretion of calcium was 350 mg. during cortisone therapy on a diet containing 137 mg. of calcium.

Discussion

Although the disease was generalized, the most important functional impairment in this case was the renal insufficiency. This was evidenced by the poor tubular secretion of phenolsulfonephthalein and the lack of ability to concentrate. As noted, the blood urea nitrogen was normal. Although massive involvement of the kidney by sarcoid granuloma has been reported, the occurrence is rare, and associated functional impairment is not described.[4] When renal insufficiency occurs in sarcoidosis, the most consistent mechanism has been nephrocalcinosis.[1] In view of the markedly elevated serum calcium in the case described above, nephrocalcinosis was considered the likely renal lesion.

Hypercalcemia has been reported in 20 to 45 per cent of the cases of sarcoid in the literature.[1, 5] The mechanism of elevation of the serum calcium is obscure. The level of serum calcium does not correlate with either bone lesions or abnormality of serum proteins.[1, 5, 6] Characteristically, the serum inorganic phosphorus remains normal, excluding hyperparathyroidism.[1, 6, 7] The danger of persistent hypercalcemia is in precipitation of calcium in the body tissues, particularly in the urinary tract in the form of renal calculi or calcinosis of the collecting tubules.[6, 8, 9]

If the serum calcium can be decreased to normal early in the process, the nephrocalcinosis is reversible. However, if the process continues uninterrupted, renal insufficiency, uremia and death may result.[1, 8]

Although, as noted above, the cause of hypercalcemia in sarcoid is not known, the serum calcium has been found to correlate with activity of the disease, an increase during exacerbations and a return to normal with remissions having been described.[10] It seemed reasonable, therefore, that any therapy that might diminish the activity of the disease might lower the level of serum calcium. With this in mind, the patient was treated with cortisone — both ACTH and cortisone have been found to decrease the lesions of sarcoid, although the results are variable and frequently, but not always, an exacerbation follows cessation of therapy.[11] In this case a prompt fall in the serum calcium to normal levels occurred. The level remained normal after cessation of therapy for a follow-up period of six months. Whether the renal function will improve over a longer period is uncertain.

Since the study of this case in September, 1952, a report of the response of hypercalcemia in sarcoid to adrenocortical hormones has appeared.[12] Three cases are described in which an elevated serum calcium fell to normal with ACTH or cortisone therapy. One patient died of renal failure ten days after treatment, and widespread focal calcification in the renal tubules was found at autopsy. Another patient did not return for adequate follow-up examination. The third patient was given four courses of hormone therapy. The serum calcium fell from 14.5 to 9.8 mg. per 100 cc. after the first course of ACTH; eight months later the serum calcium was found to have risen to 13.8 mg. per 100 cc. A course of cortisone produced a fall to 10.9 mg. per 100 cc., and when the patient was seen on two subsequent occasions, five months and a year later, the serum calcium was normal without treatment. Improvement of renal function occurred in this case over the twenty-one-month period of observation.

These facts indicate a need for serum calcium determinations in patients with sarcoid, for persistent, unrecognized hypercalcemia may lead to renal insufficiency. Whether cortisone will consistently correct the metabolic defect remains to be proved.

Summary

A case of sarcoidosis with hypercalcemia and renal insufficiency is presented. Therapy with cortisone resulted in a return to normal of the serum calcium.

The dangers of persistent hypercalcemia are discussed. Determination of serum calcium in cases of sarcoid is suggested.

Treatment with ACTH or cortisone may be indicated in cases in which hypercalcemia is found, if further study confirms the findings presented.

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MEDICAL PROGRESS

THE MEDICAL MANAGEMENT OF ARTERIAL HYPERTENSION (Concluded)*

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BOSTON

Potassium Thiocyanate and Sodium Nitroprusside

Since Barker,[124] in 1936, demonstrated that many of the toxic effects of thiocyanate administration could be controlled by measurement of the blood level, the use of this drug in hypertension has had some acceptance. The necessity of serum level determinations at intervals of two to four weeks has limited its use, but it has been recommended,[125] especially for control of hypertensive headaches. It has been reported to have increased effectiveness after sympathectomy.[126]

A recent revival of interest[127] has followed the suggestion that thiocyanate exerts its hypotensive behavior through some hormonal mechanism rather than some nonspecific vasodilating action. The drug has been found to penetrate the liver and thyroid gland as well as the adrenal gland.[128] Large doses cause disappearance of lipid granules from the zona glomerulosa of human and canine adrenal cortex, as well as atrophy.[126] Moreover, there is a small but distinct fall in serum sodium level[129] before the hypotensive action becomes apparent, and simultaneously there is increased loss of sodium in the urine. Thus, it is likely that thiocyanate exerts its hypotensive effects through a depression of the adrenal cortex. It has been known for some time that it has an antithyroid action, causing a decrease in basal metabolic rate, in some cases even to myxedematous levels,[124] and it may induce goiter formation.[130] In addition, long-continued administration may lead to osteoporosis.[131]

The dosage of thiocyanate is 0.15 to 1.3 gm. daily, most patients requiring 0.3 to 0.6 gm. a day, with determinations of blood level at first weekly and then every three or four weeks. Satisfactory blood levels are stated to be 8 to 12 mg. per 100 cc.[124] Hines,[132] surprisingly enough, considers levels up to 15 mg. per 100 cc. safe, but toxicity is common even at levels below 12 mg. per 100 cc. Toxic symptoms include weakness, somnolence, nervousness, tinnitus, skin rashes, nausea, vomiting, diarrhea, anemia and goiter. At levels over 12 mg. per 100 cc., one may also see mental symptoms such as disorientation, confusion, hallucination and coma, and death may ensue.

Since excretion of thiocyanate ion parallels chloride excretion,[133] smaller doses will be needed if the patient is also on a low-sodium diet. Persons with renal insufficiency and those over sixty years of age, or with central-nervous-system vascular disease, congestive heart failure or blood dyscrasias, should not receive thiocyanate.

These new data about thiocyanate, although giving a better understanding of its possible action, have not altered the practical difficulties of frequent measurements of blood levels and the occasional occurrence of toxic reactions despite such control. Nevertheless, satisfactory lowering has been obtained in a considerable number of cases.[127] The use of sodium nitroprusside is being studied by Page.[122] It is converted after a time to thiocyanate in the body and is believed to have a greater hypotensive effect than thiocyanate. This may be due, however, to the high blood levels of thiocyanate (12 to 20 mg. per 100 cc.) that have been found. The toxic effects usually seen with thiocyanate (drowsiness, anorexia, rashes, slight anemia and mental confusion) have been observed with sodium nitroprusside.

Hexamethonium

The demonstration by Acheson and Moe,[134] in 1946, that tetraethyl-ammonium ion blocked ganglionic transmission and thereby caused a fall in blood pressure stimulated a search for similar agents suitable for use in hypertension. The most effective drugs of this type thus far available are the pentamethonium (C_5) and the hexamethonium (C_6) compounds, both members of the polymethylene bistrimethyl-ammonium series,[135] the C_8 compounds being slightly more active.[136, 137]

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The name of methonium compounds for members of this series has been approved by the British Pharmacopoeia Commission. The general formula is as follows:

$$\begin{array}{l} CH_3 \diagdown + \qquad\qquad + \diagup CH_3 \\ CH_3 - N - (CH_2)_n - N - CH_3 \\ CH_3 \diagup \qquad\qquad \diagdown CH_3 \end{array}$$

For pentamethonium n = 5, and for hexamethonium n = 6 and so forth. Although these compounds were synthesized many years earlier, their pharmacologic and clinical potentialities were first pointed out by Paton and Zaimis[138] in 1948. These workers also presented proof in animal experiments[139] that C_5 and C_6 acted by a specific paralysis of transmission at the ganglionic synapse and not on postganglonic or preganglionic structures. The effector organs are still capable of responding. This explains (and also follows from) the fact that C_6 lowers blood pressure without diminishing the pressor response to sympathomimetic amines, that it paralyzes salivary-gland secretion from nerve stimulation without affecting that due to carbamyl choline, and that it reduces gastric secretion from vagal stimulation, but not from histamine.[140] Whereas both C_5 and C_6 are potent blocking agents competitive for acetyl choline at the ganglionic synapse, they have practically no blocking action at the neuromyelin junction. The decamethonium compound (C_{10}), however, blocks neuromuscular transmission[141] and is a powerful curare-like agent.[142]

The properties of hexamethonium in man can largely be deduced from the specificity of its ganglionic blockade.[135] Orthostatic hypotension and compensatory tachycardia occur in almost all patients (normal as well as hypertensive) because of the inhibition of sympathetic activity necessary for integrity of the postural vasomotor reflexes. During this postural fall in blood pressure, the systolic decrease is greater, the heart rate increases, and the volume of the lower portion of the body rises.[143] Venous pressure diminishes in normal persons and in those with congestive heart failure. Both the hypotension and the tachycardia are completely counteracted if the patient is immersed to the chin in a swimming pool.[143] It appears that the fall in blood pressure results from a decrease in the ability of the vessel walls in dependent parts of the body to contract and resist the pressure dilatation from gravity. Thus one of the important homeostatic mechanisms of the body, normally mediated by sympathetic pathways, has been inhibited. This should not be considered a side effect of hexamethonium; postural hypotension is one of the most important elements in its action. When a fall in the blood pressure in the supine position occurs it is presumably due to interruption of abnormal sympathetic vasoconstriction. When there is no effect on the blood pressure with the patient supine, the hypertension is regarded as being maintained by humoral factors. Apparently, the hypotension does not interfere with renal function if it is normal, but poor renal function is adversely affected.[144]

Persons receiving hexamethonium in adequate dosage have a lowered tolerance to a variety of stresses (as Cannon's sympathectomized dogs and cats did), such as anesthesia[145, 146] and hypoglycemia.[146] If a diabetic patient has a hypoglycemic reaction while under the influence of C_6, he may pass into coma without any of the characteristic anxiety, palpitation, hunger, sweating or restlessness. Lower blood sugar levels may be obtained with a given dose of insulin because sympathetic activity, which ordinarily moderates and overcomes the hypoglycemia, has been rendered inactive by the hexamethonium.

Unfortunately, C_6 does not distinguish in its blocking action between sympathetic and parasympathetic activity, and, as a result, a general inhibition of autonomic activity occurs, although the degree of block is not the same in all ganglions.[135, 139] Peripheral blood flow increases, and skin temperature rises[147]; sweating is diminished or abolished.[148] Persons receiving C_6 may have elevations of body temperature in hot weather because of the inhibition of sweating.[86, 149] Interference with the pupillary reaction to light and accommodation may cause blurred vision. Decreased salivation results in a dry mouth.

Secretion of hydrochloric acid by the stomach is inhibited, both in the resting state and after insulin.[150, 151] Motility of the entire intestinal tract is inhibited, and stomach and small intestine empty very slowly.[152] The effects on secretion and motility of the stomach are less if the stomach is full.[153] Not only does C_6 often relieve the pain of peptic ulcer but also its depression of secretion and motility may actually have a favorable effect on healing.[154] Nausea is common; diarrhea occurs rarely.[149] Inhibition of intestinal activity often results in constipation and occasionally in paralytic ileus[155-157] and even death.[158-160] Urinary retention may result and, in the presence of prostatic hypertrophy, can be quite serious. Impotence may occur, but since the effect of any dose is limited to several hours, omission of a dose will generally overcome this difficulty.

All these undesirable side effects have not prevented an extensive clinical trial.[137, 147, 148, 161-184] In England and New Zealand major interest has been in the parenteral use of C_6. In the United States most interest has been in oral administration, particularly in conjunction or alternation with other drugs.

Administration by any route should be initiated only in a hospital where constant observation and prompt treatment of untoward effects are available. There is no way of predicting which patients will respond with a fall of blood pressure or of determin-

ing the optimal dose, except by trial and error. Although the technic of intravenous administration has been carefully described,[172] it is probably too dangerous for any but experienced workers. Within fifteen to thirty minutes of the subcutaneous administration of a suitable dose there is a variable reduction in blood pressure in the supine position and increase in heart rate, with a consistent postural hypotension. The effects wear off in four to eight hours. Since most investigators agree that the greatest danger of severe hypotension exists with the initial dose,[172] this should not exceed 2.5 mg. of the hexamethonium ion.* Increments of 5 to 10 mg. are added until a suitable response (that is, postural hypotension) is obtained. Continuation of this dose, often self-administered, two to four times daily for long periods, is being used therapeutically in both England and New Zealand.[181, 167] Tolerance develops quite rapidly, and doses must be increased up to 100 mg. or more.[172] If the drug is interrupted for a few days, tolerance is lost, and resumption with the previous dose will cause profound hypotension. Freis[172] believes that tolerance is delayed if injections are given only twice daily, another hypotensive drug being given alternately. Some patients must lie down during the hour or two of maximal postural hypotension after each injection unless elastic stockings and abdominal binders are worn. Smirk[165, 167] recommends that his patients sleep with the head of the bed elevated to maintain the postural hypotensive effect.

Because of the obvious disadvantages of repeated parenteral injections, many studies utilizing oral administration have been made.[169, 177, 179, 181-183] It is clear that more patients can be controlled with parenteral than oral administration, only about 1 in 4 or 5 responding suitably to oral administration.[179] The initial dosage is 125 mg. three or four times daily, each dose being gradually increased by increments of 125 mg. until daily doses of 2 to 4 gm. (in some cases, 6 gm.) are being taken. As with parenteral administration, this should be started in a hospital with frequent measurement of blood pressure. For oral administration neither the iodide nor the bromide salt should be used. The former may cause skin eruptions; the latter has produced bromidism.[182] The chloride or bitartrate avoids these dangers.

Absorption from the intestinal tract is poor, usually amounting to about 5 to 10 per cent of the dose (urinary excretion being used as an index)[185, 186]; it is also erratic, varying from 0.2 to 34 per cent of a given oral dose. Absorption is greater when the drug is given on an empty stomach.[187] From 60 to 70 per cent of a dose can be recovered unchanged in the stool.[185, 187] The renal clearance of C_6 is close to that of inulin, and it is presumably excreted by glomerular filtration.[188] Since little, if any, of the drug is destroyed in the body, and elimination is through the kidneys, it is clear why long duration of action and development of severe toxicity are common in patients with poor renal function.

The need for an oral dose approximately ten times the parenteral dose becomes of considerable concern when constipation supervenes, because marked absorption may then occur. Cathartics or cholinergic drugs such as the urethane of β-methyl choline (Urecholine) are useful measures to ensure daily bowel evacuation. Urecholine, in doses of 5 to 20 mg. daily, is of aid in avoiding urinary retention and overcoming the dryness of the mouth, as well as moderating the constipation.[172, 181]

In evaluating a hypotensive agent as potent as C_6 one needs no placebo controls. In fact, in its marked potency lie most of its dangers. A severe and prolonged hypotensive episode with this drug (as may readily occur during oral administration associated with constipation or initially with parenteral administration) may be very serious. The dangers of fainting and of cerebral or coronary thrombosis are obvious. One can best treat severe hypotension by raising the legs and keeping the head low. Vasopressor drugs, such as norepinephrine, may be infused intravenously. Epinephrine is contraindicated[185] as it is in severe hypotension from tetraethyl-ammonium.[189, 190] It should be noted here that patients with paralysis of autonomic activity will over-react to any vasoactive drug. A vasopressor drug will cause more rise of blood pressure than expected, and a vasodilating drug more fall, because in both the compensatory mechanisms that normally moderate these blood-pressure changes are inoperative.

Since hypertensive patients are commonly exposed to more than one type of treatment, it must be kept in mind that persons with previous sympathectomy and those on low-sodium diets appear to be more sensitive to the hypotensive action of C_6.[172]

If diet and milder drugs are ineffective, C_6 alone or together with diet or other drugs may be indicated in certain patients. Patients with uremia or severe cerebral or coronary atherosclerosis should probably not receive the drug under any circumstances. Turner[189] states that no patient should have sympathectomy until C_6 has been tried and that every patient with malignant hypertension should receive it. There can be little doubt that C_6, used in the right patients and with due precautions for its potent action and side effects, can induce remarkable subjective and objective improvement in many patients with hypertension. Persons under fifty years of age with a minimum of vascular disease are probably the best subjects. The etiology of the hypertension is of no consequence. If a significant fall in blood pressure is achieved without too much ill effect from the other manifestations of C_6, improvement will usually follow. Smirk[184]

*100 mg. of hexamethonium ion is equivalent to 135 mg. of hexamethonium chloride, 179 mg. of hexamethonium bromide, 225 mg. of hexamethonium iodide or 247 mg. of hexamethonium bitartrate.

reported disappearance of papilledema in 4 and improvement in 3 of 8 patients with malignant hypertension. Freis et al.[191] reported remission of the malignant phase in 11 of 15 cases. Of 15 patients with malignant hypertension treated by Schroeder,[149] 13 were helped. Such results are most striking when viewed against the rare occurrence of spontaneous remission in malignant hypertension.[120] Headache and dyspnea improve; pulmonary edema may be decreased or resolved.[191] C_s has been reported of use in a few cases of toxemia and eclampsia, in 1 case terminating status eclampticus and permitting birth of a live baby.[192]

For continuous use the patient must be educated to all the possible harmful effects and for increased safety (as recommended by Schroeder) the blood pressure should be determined before each dose. Certainly some credence must be placed on a large number of optimistic reports. Nevertheless, its dangers have caused some experienced workers[97] in this field to abandon the use of hexamethonium.

Hydrazinophthalazine

In 1950 Gross, Druey and Meier[193] described a new group of substances with hypotensive activity. The most active of these was 1-hydrazinophthalazine (Apresoline or C-5968), which has the following structure:

Initial interest in this substance was stimulated when Reubi[194] observed that the fall in blood pressure was accompanied by an increase in renal blood flow.

The exact mechanism of the hypotension from hydrazinophthalazine is not yet clear, despite many physiologic studies.[193-199] The ability of phthalazine derivates to inhibit histaminase does not parallel hypotensive activity.[200] The vasodilator action is largely central since it does not occur in spinal cats and dogs.[193, 198] The drug has variable degrees of adrenergic blocking power in different animal species,[193, 196, 199-202] and this blockade is partly peripheral.[200] In man it inhibits the cold-pressor response and Valsalva overshoot[195, 196] (as do sympathectomy, hexamethonium, Dibenamine and dihydroergocornine) and causes some degree of postural hypotension and tachycardia. Hypotensive doses (0.3 mg. per kilogram of body weight intravenously) inhibit the pressor response to epinephrine and nor-epinephrine, this action being somewhat more effective against epinephrine.[195-197, 204, 205] Although "epinephrine reversal" has not been seen in man,[196] it has been reported in the rat, cat[182] and dog.[204] There is no rise in skin temperature[195, 207] as after Dibenamine.[100] Cerebral resistance in hypertensive subjects diminishes during the hypotensive period.[208] Hydrazinophthalazine has, in addition, the unusual property of being able to inhibit the pressor substance elaborated by the central nervous system, recently described by Taylor, Page and Corcoran,[209] as well as other humoral pressor agents (angiotonin,[210] serotonin,[209] pherentasin[149] and sustained pressor principle[210]).

The increase in renal blood flow,[211] responsible for some of the initial interest in this drug, occurs in normal as well as hypertensive persons and is not accompanied by an increase in glomerular filtration rate[207] or glucose T_m.[206] Until recently, renal vasodilatation of this degree was noted only in pyrogen hypotension[212]; vasodilatation of smaller degree has now been reported from hypotension with protoveratrine.[59] The renal vasodilatation from hydrazinophthalazine occurs in association with increased cardiac output. In fact, in man, the increase in cardiac output is 110 per cent, whereas renal blood flow increases only 40 per cent; the kidney actually does not get its proportionate share of the increased output of the heart.[207] In dogs the increase in renal blood flow is roughly proportional to the increased cardiac output.[206] The mechanism of the tachycardia and increased cardiac output is not clear. There is no direct stimulating action on the heart of a heart-lung preparation.[197] However, there is some evidence in dogs that the tachycardia is either the result of central stimulation or a direct effect on the heart.[197] Although in man the tachycardia is to some extent reflex because of the vasodilatation and fall in pressure, in animals it can be shown that the heart rate and cardiac output increase before the blood pressure falls.[206] Since the degree of compensatory tachycardia is not sufficient to explain the rise in cardiac output, there must be an increase in stroke volume. These cardiodynamics resemble those of epinephrine after Dibenamine blockade.[207]

Recent clinical reports[201, 213-215] agree that hydrazinophthalazine is an orally effective hypotensive agent of moderate potency. Its effectiveness seems to be greater in patients with milder forms of hypertensive cardiovascular disease,[214, 215] although some patients in the malignant phase have responded well with reversal of the syndrome.[122, 201] Normotensive levels have been achieved in a few[201] to 25 per cent[214] of cases. Moderate but significant decreases, especially of the diastolic pressure, have been reported in half[214] to two thirds[201] of the cases. The responsiveness of sympathectomized patients has been described as similar to that of other hypertensive persons[214] or greater.[201] Patients with neurogenic hypertension are said to be more responsive than those with "renal hypertension."[201, 214] Improvement in the cerebrovascular status of patients has been evidenced by decrease in arteriolar constriction, disappearance of retinal hemorrhages and improvement in hypertensive headache and encephalopathy.[214] The findings are consistent with the reported diminution in cerebrovascular re-

sistance after intramuscular injection of hydrazinophthalazine[206]; the percentage decreases were similar to those noted after intramuscular injection of dihydroergocornine[114] and intravenous infusion of protoveratrine.[78]

In contrast to the favorable effects on cerebrovascular symptoms is the comparative lack of improvement in the cardiac status,[214] presumably related to the increase in cardiac output. Taylor et al.,[214] in a careful evaluation of the drug in 97 patients, reported the initial appearance of congestive heart failure during treatment with hydrazinophthalazine in 2 patients and the appearance of angina pectoris in 2, when the pressure was lowered to normal. Decreased dosage so that the diastolic pressure did not fall below 100 was attended by disappearance of the angina. In 1 case an infarct developed while the blood pressure was maintained at a normal level. There were 2 sudden deaths, 1 presumably from myocardial infarction. Schroeder[201] noted the occurrence of angina pectoris in 1 of 50 patients treated. These findings are of particular interest since it has been shown that hydrazinophthalazine has a coronary dilatory action in the dog heart-lung preparation[216] and in the cat heart in situ[217] sufficient to overcome the coronary vasoconstricting action of Pitressin. Presumably, therefore, in the patients described, fixed obstructions to the flow of blood exist in the coronary vessels to such an extent that a low pressure is unable to supply sufficient blood. As further evidence that heart disease was not improved, patients who required salt restriction or digitalis did not lose these requirements during periods of blood-pressure lowering from hydrazinophthalazine.[214]

Side effects, which were noted by all workers with this drug in about two thirds of patients, were occasionally severe enough to require omission of the medication. Most severe symptoms either disappeared in three to six weeks or were adequately controlled by other drugs. Headache occurred in about 40 per cent of the patients[201, 214, 215] and was sometimes severe enough to cause the drug to be discontinued. Control of the headache could occasionally be achieved by antihistaminic drugs or by ergotamine tartrate.[215] In a series of 97 patients[214] anorexia and nausea occurred in 35 per cent and vomiting in 15 per cent, sometimes of such severity as to result in weight loss. Edema of the eyelids and ankles (15 per cent), palpitation (14 per cent), giddiness (5 per cent) and angina pectoris (5 per cent) were also seen. In 12 per cent a drug reaction characterized by malaise and muscle and joint pains appeared and in some was associated with high fever. Postural hypotension and tachycardia was so characteristic[201] that it could scarcely be considered a side effect. It was most marked early in treatment, becoming less as treatment was continued. Mild decreases in hemoglobin apparently occurred, but there were no severe anemias in 97 patients followed for more than eighteen months.[214] Serous otitis media has been observed as a complication of therapy.[88, 201]

The drug is given gradually, usually beginning with 10 mg. four times a day, after meals and at bedtime. If there are no untoward effects the dose is raised gradually in increments of 10 to 50 mg. at four-day intervals up to a maximum of 800 mg. a day, or until a good hypotensive effect appears. Thereafter, it is often possible to lower the dose and maintain a hypotensive effect.[214, 215] Schroeder[201] recommends dosage increases at weekly intervals, and points out the likelihood of reappearance of side effects, such as headache, with each increase in dose. Since some favorable responses required four or five weeks, administration should be continued for this length of time before being considered ineffective. When the drug was omitted and placebos substituted, the pressure began to rise in two to four days. As with most hypotensive drugs, withdrawal should be gradual if a hypotensive effect has been achieved, because severe exacerbation of hypertension may result.[201]

Hydrazinophthalazine appears to be a moderately effective hypotensive agent in the milder forms of hypertension, but its effects on cardiac output suggest that it will not be very useful in patients with hypertensive and cardiac disease. Longer observation will be necessary to demonstrate whether hypotension with this drug will prevent hypertensive complications and increase survival rates. Further work will be necessary to clarify its mechanism of action as well as its role in the treatment of chronic hypertension.

Combinations of Drugs

Characteristic of almost all the hypotensive measures mentioned has been their effectiveness in only a fraction of the patients treated. As yet there have been no studies indicating whether the third of patients with good results to one drug are the same third that respond well to another, or whether one can, by trial and error or by suitable combinations, find effective treatment for most patients. The likelihood of the last possibility is suggested by a growing number of reports on the successful use of more than one hypotensive agent.[97, 149, 213, 219] Reference has already been made to the increased effectiveness of thiocyanate[126] and of hexamethonium[172] after sympathectomy, as well as the greater responsiveness of patients on a low-sodium diet to hexamethonium or veratrum.[48]

The combination of hexamethonium and hydrazinophthalazine has had a number of enthusiastic proponents, although one of the companies selling these drugs states, "Use of such combined therapy except for investigational purpose is not at this time recommended. . ."[220] The rationale depends on the use of hexamethonium to inhibit the effects of neurogenic sympathetic stimulation and of hydra-

zinophthalazine to inhibit potential humoral pressor agents. Schroeder[149] stated that "the elevated blood pressure in benign hypertension was controlled at normotensive or near normotensive levels in almost every case. The malignant stage reversed itself in 18 of 20 cases." However, he also noted that, in an experience with 120 cases,[221] the course of chronic renal insufficiency was unchanged. Too rapid lowering of blood pressure precipitated uremia in 2 of 35 patients with malignant hypertension; the low-salt syndrome occurred twice in patients with malignant hypertension and nitrogen retention although salt was not restricted. Six deaths occurred under treatment, 2 presumably from hexamethonium poisoning. Sudden withdrawal of the drugs usually precipitated severe hypertensive disorders such as pulmonary edema, apoplexy, uremia and encephalopathy.

Just as the hypotensive effects are increased by the use of hexamethonium and hydrazinophthalazine together, the dangers increase.[222] The characteristic toxic reactions of both drugs appear. They should be administered alternately, never simultaneously. Schroeder[149] reported a case of sudden death in a patient who received both drugs together as an initial dose. Johnson, Freis and Schnaper[213] have given hexamethonium subcutaneously at intervals of eight to twelve hours and hydrazinophthalazine orally. Schroeder[149] has used hexamethonium orally in three or four daily doses alternating with oral administration of hydrazinophthalazine. Conclusions vary from enthusiasm [149] to moderation. Hilker, Rhoads and Billings,[219] with experience in 100 patients, state that hydrazinophthalazine is a safe, moderately effective drug with a high incidence of usually transient toxic effects and that hexamethonium is a powerful but dangerous drug.

The ganglionic blocking action of hexamethonium would be expected to interfere in the reflex action of the veratrum esters, and this would not appear to be a useful combination. However, hydrazinophthalazine and veratrum[97] or protoveratrine[98] appear to be a useful combination. The veratrum esters tend to counteract the tachycardia from hydrazinophthalazine. *Rauwolfia serpentina*, the least toxic of all these agents, appears to have a useful synergistic action with hydrazinophthalazine and with veratrum. Wilkins[97] has employed all three orally in ambulant patients with significant effectiveness, and without the attendant dangers of ganglionic blockade. The results of prolonged clinical trial with these various combinations will be of great interest.

Summary

There is much activity and much hope in the search for useful hypotensive drugs. It is already quite clear that lowering the blood pressure without too gross disturbances in homeostatic mechanisms or cardiodynamics is attended by striking amelioration of many of the signs and symptoms of even the severest manifestations of hypertensive disease. It is the more remarkable that even drugs that disturb homeostasis, such as hexamethonium, or increase cardiac output, such as hydrazinophthalazine, cause marked improvement in many hypertensive manifestations by virtue of their hypotensive action. In patients who already have cerebral or coronary atherosclerosis or severe myocardial weakness, the benefits of lowered pressure may be outweighed by sudden postural hypotension or increased cardiac output, and the pressure should not be lowered too far with these drugs. However, patients with coronary-artery disease undergoing acute hypotension with protoveratrine have shown no ill effects, presumably because there is no rise in cardiac output.

Of the hypotensive measures described, the first that should be applied is salt restriction. In nonmalignant cases it can be carried out without hospitalization. Of the drugs, the veratrum esters, hydrazinophthalazine and *Rauwolfia serpentina* may be used on an ambulatory basis. Hexamethonium, with or without hydrazinophthalazine, whether by injection or by mouth, must be initiated in a hospital. It is one of the most potent hypotensive drugs, but one with many side effects and dangers. The physician as well as the patient must be familiar with the possibility and proper management of toxic effects.

Patients who have hypertension without evidence that heart, brain or kidneys are deteriorating should probably not be treated with restrictive diet or dangerous drugs of any sort. Treatment should be reserved for those with manifestations of hypertensive disease. The others should await further clinical trial of these drugs singly and in combination. Ten years from now these medications may all be in the discard — of interest only because they have shown the way to safer and more effective agents.

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MEDICAL INTELLIGENCE

ANALYSIS OF A SERIES OF PERIODIC PHYSICAL EXAMINATIONS

NORMAN LENSON, M.D.

BROOKLINE, MASSACHUSETTS

THE following report is the result of a questionnaire submitted to a number of patients seen at the Boston Evening Clinic regarding the frequency with which they consulted physicians and dentists, and the apparent adequacy of physical examinations. It is submitted to serve as an available source of additional statistical material. No inference is intended, and no conclusions are made, since the number of patients tested is relatively small, and the geographic, social and economic factors are not considered.

A total of 350 patients consisting of 107 males and 243 females were questioned. The ages ranged from fourteen to eighty-six years, with an average of forty-three and eight-tenths years.

Thirty-two per cent of the males and 41.9 per cent of the females visited their dentists only as needed or rarely, whereas 53 per cent of the males and 50 per cent of the females were seen by their physicians under the same conditions. Sixty per cent of the males and 55 per cent of the females routinely arranged dental appointments during the period of one year, whereas 38 per cent of the males and 43 per cent of the females routinely consulted their physicians during the same period. Fifty-six per cent of the patients stated that their physicians spent thirty minutes or less during the course of their physical examination, and of these 32 per cent related that the time allotted was ten minutes or less.

Apparently adequate examinations of the eyes, ears and throat were made in 47 per cent, 39 per cent and 39 per cent of the cases respectively. The blood pressure was recorded in 82 per cent; blood tests were performed in 69 per cent, and a urinalysis was done in 71 per cent. Only 17 patients had special tests, which consisted of stool examination, electrocardiogram, basal metabolism and allergy testing. Nine per cent of 100 females had periodic pelvic examinations, and 51 per cent of the patients had yearly x-ray examinations of the chest.

TABLE 1. *Periodic Examination of Specific Body Sites.*

SITE	MALE PATIENTS		FEMALE PATIENTS	
	NO EXAMINATION MADE	EXAMINATION MADE	NO EXAMINATION MADE	EXAMINATION MADE
Chest	35 (33%)	72 (67%)	65 (27%)	178 (73%)
Hands	71 (66%)	36 (34%)	152 (63%)	91 (37%)
Feet	81 (76%)	26 (24%)	167 (69%)	76 (31%)
Breasts	79 (74%)	28 (26%)	154 (63%)	89 (37%)
Rectum	72 (67%)	35 (33%)	216 (89%)	27 (11%)
Testicles	76 (71%)	31 (29%)		
Neck	77 (72%)	30 (28%)	233 (96%)	10 (4%)
Axilla	81 (76%)	26 (24%)	213 (88%)	30 (12%)
Groin	73 (68%)	34 (32%)	233 (96%)	10 (4%)

Table 1 summarizes the examinations of specific areas of the body.

Twenty patients objected to or commented on periodic physical examination. Of these, 9 objected to the cost, and 7 stated that they thought the examinations were insufficiently thorough.

BY THE LONDON POST

Care of the Aged — The Ocular Troubles of Dr. Johnson — What's in a Name?

JOHN LISTER, M.D.

LONDON, ENGLAND

A CENTURY ago there were in Britain about 1,000,000 people (under 5 per cent of the population) over the age of sixty-five, and for every old person there were nearly 30 of working age. Today there are over 5,000,000 in this age group,

and for every old person there are only 6 of full working age. In twenty-five years the numbers over sixty-five may be above 8,000,000.

It was this problem that Parliament discussed when a private member brought a motion calling on the Government to do more for the aged sick. The motion was carried after members of all parties had contributed to the debate, and all speakers agreed that the problem was serious, although the suggested methods of solving it varied. One speaker said that the subject could certainly be discussed sympathetically in the House of Commons, some of whose members were sixty, sixty-five and over seventy years of age, and the Prime Minister himself was vigorous at the age of seventy-eight.

It was said that many beds in hospitals for the treatment of acute illness were being occupied by elderly people who could not be sent home because of mental and physical deterioration, and one member called for a geriatric unit in every hospital with more than 500 beds. Another member pleaded that hospitals for old people should not be called "hospitals for incurables," — he remembered one described as a "home for forlorn and desolate females." A different aspect of the problem was stressed by a speaker who suggested that many old people did not want to live among other old people, "waiting for funerals, the only spark of brightness in their week."

The attitude of the Ministry of Health was that the majority of people prefer to stay in their own homes and that the Government favored treatment at home. The aim was to develop the parts of the health and welfare services that would increase the comfort and care of the aged without imposing an intolerable financial burden on the community. Furthermore, the problem could not be solved by the state alone, and there was a great opportunity for voluntary work in this field.

* * *

The Royal Society of Medicine recently spent an unusual hour listening to Dr. Peter Beattie's description of the ocular troubles of Dr. Samuel Johnson. The various ophthalmic disorders from which he suffered were deduced from a study of a number of paintings of the doctor by Sir Joshua Reynolds and a perusal of his own writings and those of his biographer, Boswell.

He was apparently almost blind in his left eye from childhood, probably as a result of phlyctenular keratitis, and was shortsighted in his right eye. In fact, he is recorded as saying of himself: "The dog was never good for much." All the same, he was displeased with a portrait painted by Reynolds in 1775 showing him reading a folded-up book held close to his eyes, and he protested that he would not be known to posterity for his defects only.

There was considerable discussion about whether or not his poor vision in the right eye was due to a straightforward myopia. Shortsighted he certainly was, but he did not wear glasses, which were available at the time, and in spite of the difficulty in reading, he was able, during his tour of the Hebrides, to correct Boswell about the shape of a distant hill. It was thought that perhaps he had myopic astigmatism that could not be corrected at the time.

Apart from his myopia, Johnson suffered more than one attack of inflammation of his good eye, and among his personal writings, there is a prayer, dated 1746, that opens with the sentence: "Almighty God, who has restored sight to my eye. . ." The nature of these attacks is not clear, but he was a known sufferer from gout, and he may have had iritis, although the second attack occurred during a fever when he may simply have had dendritic ulceration.

In spite of his eminence, Johnson never consulted the most fashionable ophthalmologist of his day, Chevalier Taylor. This was apparently because he regarded him as the greatest charlatan of his time and the best example of how far impudence can carry ignorance.

In any event, during his latter years, the vision in the right eye, although never good, was adequate and not seriously affected by the hypertension, renal disease and cardiac failure that eventually brought about his death in 1784.

* * *

Harley Street and Wimpole Street have long been the Park Avenue of the London consultant physicians and surgeons. Ever since the start of the Health Service there has been speculation about the future of this corner of the West End. The gloomy prophets have forecast that within a generation the consulting rooms will have given place to offices and shops. The *British Medical Journal*, having reviewed the evidence, doubts this and believes that the "Street" is good for a long time yet.

The neighborhood was once the favored residential quarter for artists, architects and statesmen, but for the last hundred years it has been predominantly occupied by the medical profession. When the future Viscount Dawson of Penn put up his plate at the end of the nineteenth century, he is said to have been glad to pay nearly half his income for renting an apartment and consulting room in Harley Street. At that time the houses, built in early Georgian style, had a dignity in keeping with the consultant side of medical practice. The name plates on the doors have always been characteristic. They are small and usually cannot be read from below the door step, and some are so worn that the name is almost illegible. In the old days, it was considered bad taste if there were more than two or three names on each door. Today this is not so. The *British Medical Journal* reports that there are 664 door plates in Harley Street bearing medical names, 346 in Wimpole Street and many more in

Queen Anne Street, Devonshire Place and Welbeck Street. One house alone had 20 names. This would, of course, be regarded by the old-timers as a sign of decadence, as would the fact that a number of offices have invaded the area. Nevertheless, it shows that there is still a demand for private medical advice, and the London County Council, despite objections voiced at a recent inquiry, are anxious to keep the area purely medical or at least professional and residential. Furthermore, the phrase "a Harley Street opinion" still connotes in the lay mind the highest medical judgment in the land, and so it seems unlikely that these door plates will disappear in the near future.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 39221

PRESENTATION OF CASE

A forty-three-year-old single housewife was referred to this hospital with a previous diagnosis of pemphigus vulgaris.

The patient was well until about two years before admission, when she first noted a spot of alopecia with crusting on the scalp and an ulcerative, painful lesion in the oral cavity. She consulted a number of physicians, who prescribed a variety of medications, but none gave her relief. The oral lesions cleared up within a month but later returned, and a diagnosis of pemphigus vulgaris was made.

Seventeen months before admission she had been treated with ACTH (adrenocorticotrophic hormone), 200 mg. intramuscularly daily, for the first time. Later, ACTH was given intravenously. Her subsequent course was marked by remissions and exacerbations with the development of new lesions, for which during most of this seventeen-month period she was in and out of the hospital. During almost every hospitalization she was treated with ACTH. Four months before admission she was found to have hyperglycemia and glycosuria for which she was given 20 units of insulin daily. Despite various programs of therapy with ACTH, extension of the disease developed, and she was referred to this hospital.

Physical examination showed an obese patient with conspicuous features of Cushing's syndrome. There was muscular weakness, hoarseness, round, full, plethoric facies, girdle obesity, mild hirsutism, acneiform lesions on the face and upper chest, easy bruisability, and purpuric areas on the axilla and back. Superficial ulcerative lesions were present over the neck, chest, back, abdomen and groins. There were occasional minute vesicles over the chest and neck regions and a few secondarily infected bullae. The mouth and tongue were covered with white, shallow erosions. The heart, lungs and abdomen were normal.

The temperature was 99.5°F., the pulse 90, and the respirations 20. The blood pressure was 140 systolic, 90 diastolic.

The urine had a specific gravity of 1.035 and gave an olive test for glucose; the sediment was normal. Examination of the blood revealed a hemoglobin of 18.2 gm. per 100 cc. and a white-cell count of 13,400, with 84 per cent neutrophils, 13 per cent lymphocytes, 2 per cent monocytes and 1 per cent basophils. The hematocrit was 54 per cent. The eosinophil count was 3 per cubic millimeter. The serum sodium was 137.3 milliequiv., the potassium 5.0 milliequiv., the carbon dioxide 27.5 milliequiv., and the chloride 100 milliequiv. per liter; the nonprotein nitrogen was 24 mg., and the fasting blood sugar 201 mg. per 100 cc. A stool guaiac test was negative. An electrocardiogram was normal, as was a roentgenogram of the chest. The spine did not show obvious osteoporosis or any other abnormality except for early degenerative changes in the mid-dorsal region. A biopsy of the skin confirmed the diagnosis of pemphigus.

The patient was given 1 or 2 gm. of terramycin daily. ACTH therapy was as follows: ACTH gel, 80 units every day for two days, ACTH intravenously, 40 mg. every day for eight days and 60 mg. every day for twenty-three days; and ACTH gel, 120 units for two days, 240 units for fifteen days, 120 units for one day and 60 units for two days. The skin and oral lesions seemed to improve; however, during the fourth week in the hospital back pain developed. A roentgenogram of the spine revealed a compression fracture of the bodies of the twelfth thoracic and first lumbar vertebras (Fig. 1). The mental status of the patient altered, and she became more hostile, demanding and uncooperative. Because of these symptoms all ACTH therapy was stopped. On the following day, marked muscular weakness developed with a decrease of blood pressure to a level so low that at one time it was not obtainable. The temperature rose to 102°F., and several blood cultures grew out *Staphylococcus aureus*. The serum sodium was 130 milliequiv., the

potassium 4.7 milliequiv., and the chloride 96 milliequiv. per liter; the serum nonprotein nitrogen was 41 mg. per 100 cc. An electrocardiogram disclosed that the T waves were inverted in Lead 3 and flat in Lead aVF, but there were no other changes. The fever persisted; the blood pressure returned but remained low. The pulse was weak and feeble. The patient died during the ninth week in the hospital, three days after ACTH had been stopped.

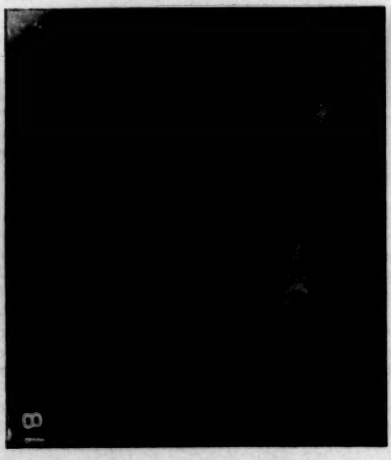

FIGURE 1. *Roentgenogram of the Spine. Arrows point to fractures at the bodies of the twelfth thoracic and first lumbar vertebrae.*

DIFFERENTIAL DIAGNOSIS

DR. DALTON JENKINS*: The diagnosis of pemphigus was established on clinical grounds and confirmed by biopsy; therefore, this diagnosis is accepted, and it may be assumed that the skin lesions did not represent the bizarre or complicating manifestations of systemic disease.

The patient was given intermittent intramuscular injections of ACTH, a method for the treatment of pemphigus that has been widely and successfully used and has been thoroughly described by Dr. Lever.[1,2] The objective is to treat the patient intensively for short periods, to withdraw the ACTH and thus to provide periods of escape from the side effects produced, and then to readminister the hormone before severe fulminating relapses of the skin lesions can occur. That the disease continued to be active is reflected in the presence of fever and tachycardia, although both those symptoms may have been evidence of complicating infection, to which high levels of steroid therapy predispose. Certainly, a staphylococcal septicemia ultimately developed since repeated blood cultures grew out *Staph. aureus*.

The hyperglycemia and glycosuria that developed four months before admission presumably reflected a poor reserve function of the beta cells of the pancreas. Because of the comparative rarity of steroid diabetes, it would be interesting to know whether the patient had a family history of diabetes mellitus. Apparently, the diabetes resulted from the continued administration of large quantities of ACTH, but fortunately could be controlled by only 20 units of insulin. Frequently, considerably larger doses of insulin may be required for the regulation of steroid diabetes.

When the patient entered the hospital, she was in good chemical balance despite the intensity and duration of adrenocortical stimulation; therefore, I assume that she had been receiving supplementary potassium and perhaps testosterone, although they were not mentioned. Actually, the potassium level of 5 milliequiv. per liter makes me wonder about the state of renal function, for if renal function is good, large doses of potassium are well tolerated. The high hematocrit and high hemoglobin could have represented dehydration or could have been another manifestation of the Cushing syndrome induced.

It would be helpful to know the type of ACTH that was used.

DR. WALTER F. LEVER: Wilson's gel was used.

DR. JENKINS: The units described, then, are the so-called clinical-equivalent units. The actual dosage of ACTH is obviously important in establishing the degree of adrenocortical stimulation produced. Two hundred and forty clinical units of an ACTH gel means not 240 *U.S.P.* units of ACTH dissolved in gelatin, but approximately 80 to 120 *U.S.P.* units of ACTH dissolved in gelatin. The clinical effect of one injection of a given dose of ACTH gel, however, is roughly equivalent to that of the intermittent intramuscular injection of the same number of *U.S.P.* units of lyophilized ACTH dissolved in saline solution. Let me clarify that. Since the intensity of adrenal activation produced by a given dose of ACTH varies directly with the duration of stimulation, the effect of ACTH that has been placed in a long-acting menstruum is considerably greater than that of an equivalent dose given in saline solution. Therefore, the commercial products are labeled in terms of the clinical effect and not in terms of the actual number of *U.S.P.* units in the vial.

This patient received large doses of ACTH, which were increased as time went on to a final dosage level of 240 clinical units per day. That is really

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an immense dosage of ACTH gel. That these large doses were necessary suggests either that the disease was not responding or that the adrenal cortex was not responding. It has been well proved that adequate control of pemphigus often requires extremely large doses of either ACTH or the steroid hormones themselves. There is frequently no way to explain why some inflammatory lesions respond to a given dose and other inflammatory lesions do not. Probably the best example of the failure of an inflammatory lesion to respond to steroid hormones is acute nephritis, which not only is quite refractory but also may well be aggravated by the administration of steroids. Whatever the reason, pemphigus usually requires large doses of ACTH for adequate control and indeed in some patients may not be completely controlled by any dosage level that has yet been administered. However, the disease in this patient certainly improved.

Was the adrenal cortex responding? The patient entered the hospital with the stigmas of Cushing's syndrome, which must have been produced by the ACTH; therefore, the adrenal cortex had responded. Patients who are seriously ill may require larger quantities of ACTH for a given quantitative level of response than normal persons. In his studies Dr. Lever found that even by intravenous administration, 40 or 50 units of ACTH may be needed to give the same effect in patients with severe pemphigus that a dose of 20 units obtains in a normal subject. Since this was a highly purified preparation of ACTH, I am sure that the ACTH was being adequately absorbed and was being effective.

May we see the x-ray films, please?

DR. STANLEY M. WYMAN: The original film of the chest shows no active disease. The early films of the thoracic and lumbar spine demonstrate no striking changes. There is perhaps slight demineralization of bones for a patient of forty-three years of age. The compression fracture is well seen at this point involving the body of the first lumbar vertebra, and to a lesser extent there is compression of the twelfth thoracic vertebra (Fig. 1). At this time the bones may be somewhat more demineralized but certainly not strikingly so. The patient had one gastrointestinal examination, which was not remarkable. The spleen may be slightly prominent. There is a small hiatus hernia.

DR. JENKINS: You see nothing inconsistent with the diagnosis of a compression fracture secondary to osteoporosis?

DR. WYMAN: No.

DR. JENKINS: One of the most unfortunate side effects of intensive adrenocortical stimulation or intensive steroid-hormone administration is osteoporosis. That this is a true osteoporosis has been well demonstrated by the studies of Albright and Reifenstein.[3] In our experience a period of thirty days is short for a compression fracture to develop. When a compression fracture occurs secondary to osteoporosis, which is secondary in turn to the administration of steroid hormone, one wonders about the possibility of underlying bone lesions that may have facilitated this event. It was not stated whether the menopause had occurred in this patient, and the menopause could have contributed to the previous development of osteoporosis. Presumably, she was immobilized during at least part of her therapy, and that could also have predisposed her to the development of osteoporosis. On the other hand the evidence on the original films of some thinning suggests that the prior course of ACTH given over many months had already produced some osteoporosis before admission to the hospital. Certainly, the degree of adrenocortical stimulation in this patient must have been extreme.

In the hospital the patient exhibited some alterations in personality, and the ACTH therapy was stopped. Although it was not so stated, treatment was apparently terminated suddenly. I know of no more uncomfortable position to be in than to have to choose between dealing with a prolongation of a psychotic state while the hormone is continued or tapered slowly and dealing with the effects of acute hormone withdrawal. Because the psychotic state is reversible and because the effects of acute hormonal withdrawal, especially in patients who are seriously ill, may not be reversible, we ordinarily take the course of tapering the drug and dealing with the psychosis in the best manner possible. After withdrawal of the ACTH the patient demonstrated marked muscular weakness, hypotension and an increase in fever, all of which could well have been due to hormonal withdrawal with a resultant relative adrenal insufficiency. During that time the serum electrolytes were normal although the nonprotein nitrogen was somewhat elevated. After the sudden withdrawal of intensive ACTH therapy, patients may demonstrate severe symptoms of relative adrenal insufficiency but maintain relatively normal serum electrolytes because of a proportionate urinary loss of water and sodium, and a redistribution of electrolytes between cells and the extracellular space.

The electrocardiogram revealing that the T waves were elevated in Lead 3 and flat in Lead aVF gives no basis for the diagnosis of a discrete cardiac lesion. However, the incidence of occlusive vascular accidents during intensive steroid therapy, especially after withdrawal, is significant; the possibility of coronary thrombosis exists although one cannot make such a diagnosis on the basis of the nonspecific changes described.

Two problems, therefore, are crucial; the patient's death and the state of the adrenal glands. The patient had Cushing's syndrome — what might be termed iatrogenic Cushing's syndrome. It appears probable, however, that after the abrupt with-

drawal of ACTH there was a relative adrenal insufficiency in the presence of a progressive, severe, underlying disease, complicated by a generalized staphylococcal infection. Under comparable situations death has occurred, and it seems not unlikely that this sequence contributed to this patient's death. The adrenal glands probably were still large and were relatively depleted of lipid. The question of the possibility of infection, necrosis or hemorrhage in those glands arises. It has been adequately demonstrated in animals that markedly hyperplastic adrenal glands produced by the administration of ACTH are considerably more susceptible to either circulating toxins or circulating bacteria than normal adrenal glands are. My diagnoses, then, are pemphigus vulgaris, generalized staphylococcal infection and relative adrenal insufficiency.

Dr. Walter Bauer: I agree with Dr. Jenkins that hormone administration should be reduced gradually in patients on long-term therapy once they become psychotic. These psychoses are reversible in the majority of cases, whereas sudden cessation of therapy frequently has serious consequences. Psychoses alone are not adequate justification for abrupt cessation of therapy, particularly when large doses of hormone have been administered for months.

Dr. Chester N. Frazier: I should like to make one remark concerning Dr. Jenkins' statement that pemphigus is an inflammatory disease. I am not so certain that it is an inflammatory disease.

Dr. Lever: One thing that was not mentioned is that a subcutaneous staphylococcal abscess developed on the right side. The consulting surgeon wanted to open the abscess, but the patient refused to have that done. It is perhaps important to know that a staphylococcal infection was present in the system before the ACTH was withdrawn.

I think it is essential in the treatment of pemphigus with ACTH not to be too ambitious and to try to clear all the lesions. One should give sufficiently large doses to improve the lesions to such an extent that the patients are not bedridden, but one should not give large doses of ACTH too long and in this way increase the risk of ACTH damage. Retrospectively, I would say that perhaps this patient was treated somewhat too ambitiously.

Dr. Bauer: How do you feel about discontinuing hormone therapy once a psychosis appears?

Dr. Lever: I do not know whether this patient had only a psychosis. She already had an overwhelming staphylococcal sepsis; she was not merely psychotic — she was really sick and semicomatose.

Dr. Benjamin Castleman: How much antibiotic treatment was the patient given at that time?

Dr. Lever: She was receiving 1 gm. of terramycin all along; then penicillin 600,000 units a day was added during the last week of life when she had the staphylococcal abscess.

Dr. Frazier: I am not so sure that with the advantage of hindsight our treatment of this patient would have been much different. We already know that to effect a remission in this disease, we have to give ACTH in a dosage as large as or larger than that received by the patient under discussion. The problem all along was to restore the skin to reasonable integrity. I think it has been the general experience on the Dermatology Service that the treatment is a two-edged sword; the disease cuts too — which cuts the deeper I shall leave to you.

Clinical Diagnoses

Pemphigus vulgaris.
Cushing's syndrome (ACTH therapy).
Staphylococcal septicemia.

Dr. Dalton Jenkins' Diagnoses

Pemphigus vulgaris.
Cushing's syndrome (ACTH therapy).
Generalized staphylococcal infection.
Relative adrenal insufficiency.

Anatomical Diagnoses

Pemphigus vulgaris.
Cushing's syndrome (ACTH therapy).
Septicemia, Staph. aureus *with abscesses in heart, lungs and kidneys.*
Adrenal hyperplasia, severe, secondary to ACTH.
Osteoporosis, with compression spinal fractures.
Renal calcinosis.

Pathological Discussion

Dr. Castleman: At autopsy the patient had all the external characteristics of Cushing's syndrome — the moon face, the hirsutism and the various other manifestations. The most striking finding in the gross examination was in the adrenal glands, which were equal in size and together weighed 50 gm., four times the normal weight. When sectioned they were extremely hemorrhagic. The kidneys were

also large, swollen and quite hemorrhagic although the cortex and medulla were still visible. On the gross examination I thought both the kidneys and adrenal glands contained areas of necrosis.

Microscopically the sections of the skin looked almost normal. There was some hyperkeratosis and some pigmentation of the basal layers, but there were none of the characteristics of pemphigus — in other words, the pemphigus had been well controlled. The areas in the adrenal glands that we thought were necrotic and hemorrhagic were just markedly congested — the red cells were all within capillaries with little extravasation. The spine was markedly osteoporotic, with a dearth of bone trabeculae. This osteoporosis, with the patient lying in bed, had given rise to a hypercalcemia (although I could find no evidence in the clinical record of a serum calcium determination) as demonstrated in the calcium deposits in both the tubules and the interstitial tissue of the kidneys. There were numerous, small abscesses in the heart, the kidneys and lungs to go along with the staphylococcal septicemia. I think the changes in the electrocardiogram were probably due to the abscesses in the heart.

Dr. Bauer: Did you find abscesses in the vertebras that were fractured?

Dr. Castleman: No.

Dr. Bauer: Were there any changes in the brain?

Dr. Castleman: We do not have sections on the brain yet; on the gross examination it looked perfectly normal.

The changes in the pituitary gland were quite interesting, and I shall ask Dr. Burt to say something about them.

Dr. Agnes S. Burt: The pituitary gland weighed 440 mg., which is slightly below average weight, and was not remarkable grossly. Microscopical examination was extremely interesting in that the cellular picture closely resembled the findings in spontaneous adrenal hyperactivity. Table 1 shows a differential count on the cells of the pituitary gland of this patient compared with a count on a somewhat younger woman with a functioning adrenal carcinoma and with the average values for normal premenopausal women. It will be noted that both this patient and the woman with adrenal carcinoma had no normal basophils, all of them having undergone Crooke's[4] hyaline change, which is pathognomonic of Cushing's syndrome. The hypertrophic amphophils, which are also pathognomonic of adrenal hyperactivity, were increased in both women to a highly significant degree. The sparsely granulated basophils and chromophobes were normal, whereas the acidophils were somewhat low. In summary, this patient died with a small pituitary gland with a histologic picture duplicating that found in spontaneous adrenal hyperactivity.

Table 1. *Differential Counts on Cells of the Anterior Pituitary Body (Periodic-Acid-Schiff Reaction, with Orange G Counterstain).*

Age	Sex	Diagnosis	Normal Basophils	Crooke's Hyaline Basophils	Sparsely Granulated Basophils	Hypertrophic Amphophils	Acidophils	Chromophobes
yr.								
41	F	Pemphigus (ACTH)	—	7.7	4.2	6.7	26.8	54.6
25	F	Carcinoma adrenal	—	7.3	5.9	4.3	23.7	58.8
Normal premenopausal women (Meligren[3])			6.7	0.02	4.9	0.3	37.0	50.8
Probable error			0.66	0.005	0.31	0.053	2.27	2.14

Dr. Castleman: The adrenal gland was further studied by Dr. Cohen, who will describe his findings.

Dr. Richard B. Cohen: The pattern of lipoid distribution in this adrenal cortex as determined by a number of histochemical studies was similar to those we have found in the cortexes in several cases of naturally occurring Cushing's disease. The lipids were generally reduced, the cholesterol and its esters being more prominently decreased than the neutral lipids. Correlating our histochemical data with clinical and laboratory data we postulated that this was an actively stimulated, actively secreting gland that was not storing lipids. Further studies of this type will have to be carried out before definite conclusions can be drawn.

Dr. Castleman: I do not think we can decide exactly why this patient died. Whether the ACTH withdrawal was responsible or was merely an additional factor in her death is difficult to say; cer-

tainly, there was the complicating factor of a fairly severe staphylococcal septicemia, with abscesses in many organs throughout the body. Although the gross appearance and the histology of the adrenal glands were consistent with an active gland, we are not at all sure that that means the cells were functioning.

DR. BAUER: We know that previously normal people die from a fulminating septicemia of this type in a matter of hours, let alone a few days.

DR. FRAZIER: I should like to make one final remark about the compression fracture of the vertebra. During the past year, when we have been using almost entirely the depository type of ACTH, — the so-called ACTH gel, — we have had 4 compression fractures of the vertebras. In fact, when this patient was in the hospital, they were all on the ward at the same time — 2 men and 2 women. During the preceding two years when we treated as many, if not more, cases of pemphigus by intravenous infusion of ACTH in glucose solution, given over a period of eight hours daily as a rule (although in a few cases an indwelling catheter was used and the treatment lasted through the twenty-four hours), we had no case of fracture. That suggests, as has been brought out, that the continuous action of ACTH was responsible for the decalcification, whereas when ACTH was given interruptedly, decalcification did not occur. I assume that with the older types of treatment the adrenal gland had some chance to recover its function in the sixteen hours between infusions.

It is, of course, extremely difficult to determine when there is a relative adrenal insufficiency. Patients who have been given extremely large doses of hormone and develop Cushing's syndrome may, when the dose of hormone is reduced to levels that are still greater than those required for the maintenance of patients with Addison's disease, exhibit evidence of relative adrenal insufficiency. This apparently means that there is such a thing as accommodation by the organism to the circulating hormone. In reverse, one sees this in untreated patients with Addison's disease who have in some unknown way compensated for the lack of circulating steroids. One can break that compensation rapidly by administering cortisone. The presence of the structural evidences of Cushing's syndrome, therefore, need not mean that the patient does not have relative adrenal insufficiency.

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CHIROPRACTIC DEFEAT

THE House of Representatives of the General Court of Massachusetts on May 4 rejected, by a vote of 144 to 63, the 1953 bill to license chiropractors. This bill, already approved by the joint Committee on Public Health and the House Committee on Ways and Means, made provision for a special 5-man board of chiropractic registration to consist of 1 physician and 4 chiropractors. Its passage would have removed Massachusetts from the little company of 4 states, the others being New York, Louisiana and Alabama, that have so far resisted all chiropractic manipulation, regardless of the pressure exerted.

A chief argument in favor of the bill was aptly expressed as "the basic right of every human being to seek the relief he wants." If such an argument were carried to its logical conclusion not only would this bill have passed but some day it might well have been followed by acts to legalize abortion and to abolish any control whatsoever over medical practice.

This particular basic right that is attributed to every human being apparently without respect to the country in which he lives was long ago willingly surrendered by the citizens of the world's free nations. These free peoples, without exception, have voluntarily submitted to regulations imposed on them by their representative governments and designed for the common good. Every law on the books, indeed, restricts in some way the rights of some persons to do as they please.

Specifically, the right of every human being to seek the type of medical relief that he might want was restricted in this state at least as early as 1818. In that year the legislature passed an act depriving any practitioner of medicine of the benefit of law for the recovery of a debt or fee for professional services unless he had been licensed by the officers of the Massachusetts Medical Society or received a degree in medicine from the only medical school then available in the Commonwealth.

The current restrictions on the right of Massachusetts residents to seek the above-mentioned relief were enacted in 1894, when a board of registration in medicine was created by the same legislative body that now, with courage and conviction, has again upheld that act. This decision is one for which the people themselves are responsible, by virtue of having given into the hands of their representatives the responsibility and the power of determining in various matters what is in their best interests.

The defeat of the bill in question, it should be noted, did not so much deny to chiropractors the right to employ their peculiar system of treatment on the citizens of the Commonwealth as continue requiring of them the same minimum qualifications that are required of all others who wish to practice the healing art. This, it would seem, represents a degree of justice that must be obvious to all.

In the last analysis the people, under a system of free government, eventually get what they be-

lieve they want. The wishes of a majority of the people, if clearly expressed, will prevail even when opposed by powerful lobbies.

A wholesome lesson to be derived from the current repudiation of the chiropractic lobby is that of the value of education in matters concerning the health and welfare of the public. Painstaking and honest enlightenment of those who are to be affected by any legislative act is in the long run more effective than propaganda or power politics. This is not a matter of "brain washing" or of subtle indoctrination. It is a matter of placing before the people repeatedly, but sincerely, the plain facts on which they must be expected then to base their decisions.

This lesson must be taken to heart especially by organized medicine, if it is to retain the confidence of the public, so necessary for its full functioning in the public's behalf.

It may be recalled that Mark Hopkins deplored the tendency for physicians to consider the domain of medicine as solely their own and thought that the public generally should have a considerable knowledge of the laws of health. This he thought was the only guard "against the prevalence of quackery, which is found to deposit its eggs and mature its growth upon ignorance alone."*

*Farnsworth, D. L. Doctors Afield: Mark Hopkins. *New Eng. J. Med.* 248:821, 1953.

EFFECTIVE POLIOMYELITIS VACCINES

WITHIN the last three or four years a number of discoveries have raised high hopes for the ultimate solution of one of the major problems in the conquest of poliomyelitis — the prevention of its crippling effects. Some of the major accomplishments that point to ultimate success may be enumerated.

Studies of the immunologic classification of strains of poliomyelitis virus from various sources have indicated that, for practical purposes, only three varieties need be considered; they are now referred to as Type 1 for those having the Brunhilde strain as their prototype, Type 2 for those resembling the Lansing strain and Type 3 for those that resemble the Leon strain.[1]

It has already proved possible to propagate virulent poliomyelitis viruses of these three types in cultures of non-neural tissues[2] and thus to make avail ableadequate supplies of virus for immunologic studies and possibly for use in effective vaccines.

Human gamma globulin from large pools of blood plasma[3] or from human placentas[4] has been shown to contain neutralizing antibodies against poliomyelitis viruses and has already proved effective in conferring considerable protection against paralytic poliomyelitis both in laboratory animals[5] and in human beings,[6] although the protection is only brief and not absolute. The practical obstacles to the use of gamma globulin have already been stated.[7]

With the use of apparently noninfectious virus vaccines produced in tissue cultures, it has already proved possible to induce the production of antibodies against the three types of poliomyelitis in human beings to a degree similar to that resulting from natural infections; such antibodies seem to persist for at least several months.[8] Many details must still be worked out before this method is declared safe and effective and before the limits of its usefulness are defined.

There is accumulating evidence that by adapting strains of poliomyelitis to new and different living hosts one can make them avirulent and yet antigenic in human beings[9] or in susceptible primates.[10, 11] At least one of the strains has already been adapted to chick embryos,[11, 12] and if the preliminary indications of the loss of pathogenicity for monkeys is confirmed and extended to other types and to loss of pathogenicity for human beings, a much more practical source of large-scale vaccine production may become available for further study. This is by far the most promising development, but one that at the moment is farthest from full practical accomplishment. If it eventually proves successful, it may rank in importance with smallpox and yellow-fever vaccination.

Many other important contributions might be mentioned, but these will suffice to illustrate the intermediary objectives already achieved.

At present only a relatively short distance on the road to eventual success has been covered. Gamma globulin, in spite of the publicity that it has received can offer only a brief, inadequate and not very satisfactory solution of the problem. But

a beginning has been made, and it seems that a final solution is possible.

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CURRENT EVENTS

THE sometimes tedious processes of printing, except as they are applied to the daily press and the weekly news magazines, make any attempt at the journalistic discussion of current events frequently something less than current. A society accustomed to the casual contemplation of supersonic rates of speed in getting about likes to have its news not only fresh but practically raw.

Considerably out of date, therefore, is the story of federal departmental extravagance as related by a news analyst relative to the Navy's rush-order purchase of several hundred (or more credibly thousand) hastily designed lift trucks. Like insecurely harnessed dragons these engines had the built-in capacity of turning on their riders and unseating them — at times crushing them — while their insides made explosive noises and blew flames through the cracks in their armor. The Navy, fortunately, according to this source of information, was able to dispose of a number of the monsters to the purchasing officers in the Pentagon.

Only occasionally is a country as fortunate as this one in finding as a leader a military expert capable of rising above his professional training; and almost no one other than such a combination of military specialist and socially, politically and economically conscious citizen could know how to reduce a military hierarchy, even if 5-sided, to a size and shape that would permit it to fit into its proper place within the framework of a democracy.

Often reforms should be made publicly, especially when the need is great and well recognized by the public. Under these circumstances the announcement of a needed change may help to restore rather than to jeopardize further the confidence of the people in the institution in question. Perhaps this is always the best way to effect a reform, and any reference to public laundromats is entirely out of date. Announcement of a need for reform, however, should not long precede the reform itself.

Certainly the medical profession, which once shuddered at the very rustle of a newspaper, now looks upon the headline writer as someone almost human. This new tolerance of newsworthiness may have to do with the rushing of a patient to the emergency entrance of a hospital engaged in a financial campaign, the discovery of a new form of coronary-artery disease and its treatment, or a discussion of the extent to which fee-splitting has invaded a generally honorable calling.

The country has had an encouraging lesson in the use of the direct challenge for reform in the President's cordial invitation to the communist world to put up or shut up. Particularly when one's antagonists seem to bear gifts are they most dangerous. But we, as well as they, know that the race is not always to the swift; conversely, they, as well as we, know that to praise the Lord and pass the ammunition is a course of action particularly effective when there is enough ammunition to pass.

COMMERCIAL SCHOOLS OF NURSING

IN view of the well known difficulties of maintaining adequate nursing personnel and the acknowledged desirability of developing a supply of trained practical nurses in addition to a reasonable number of practical trained nurses, any steps toward promoting a satisfactory program must be viewed

with interest. One of the immediate steps in the right direction is that of reducing the number of inadequately trained and incapable nurses that are at present being poured into the field. These are the product of the many commercial schools of nursing operated for profit and without the approval of any state agency legally authorized for the purpose.

A committee to inquire into the nature and scope of the problems of commercial schools of nursing has accordingly been designated by the Joint Commission for the Improvement of the Care of the Patient and has already started to hold its meetings. Its first deliberations have been directed toward outlining the problem and determining its nature and magnitude; much of this information has already been collected and published by Dorothy Deming for the Commonwealth Fund.*

Miss Deming has found that many commercial schools admit candidates indiscriminately, without inquiring into their qualifications, to courses conducted by poorly qualified teachers with limited equipment and poor supervision. These schools, which are conducted for profit rather than for service, charge the students high rates, make doubtful claims about the students' capacities after the course, and place them in positions unsuited to their abilities. The "graduates" are, in fact, so incapable of performing the duties for which they are supposed to be trained as to constitute a grave danger to the public safety.

Many of these schools operate through correspondence courses; in fact, according to Miss Deming, there are estimated to be no less than a hundred schools or courses making claims "to prepare practical nurses through classroom lectures demonstrations, or correspondence." With one school alone claiming over 50,000 "graduates" of its twelve-month correspondence course, it can readily be seen that the lobbying strength of these institutions makes infinitely greater the difficulties of obtaining the enactment of sufficiently restrictive legislation.

As usual, when the correction of any fault is attempted, a widespread educational campaign prior to the supreme effort is the most effective instrument that can be employed. Thus it is the hope of the committee that information on such a vital problem can be spread through the American Hospital Association and the American Medical Association and that an informed body of public opinion can be developed.

*Deming, D. *The Practical Nurse.* 370 pp. New York: Commonwealth Fund, 1947.

Massachusetts Medical Society Anniversary. — *In 1854 the anniversary meeting is to be held at Fitchburg — an enterprising, beautiful town, about forty miles from Boston, and which probably is to be the next city chartered in Massachusetts.*

Boston M. & S. J., *June 1, 1853*

MASSACHUSETTS MEDICAL SOCIETY

DEAN S. LUCE, M.D.

With the sudden death on April 9 of Dr. Dean S. Luce, of Canton, the Massachusetts Medical Society has lost an active and well informed councilor who had served faithfully over the years. He was well known nationally, having been made Doctor of the Year in December, 1950, and having been invited to speak in Nashville and Los Angeles since then. His district has lost a past president who fought vigorously at every opportunity against the encroachments of bureaucracy and medical socialism. He might have made enemies had he been of a vindictive character, but his hands were clean, his outlook well based on facts as he saw them, and his speaking and writing so unemotional that his most outspoken opinion was received with respect and with little rancor.

The story has been told over and over again of his youth on Martha's Vineyard, his hard work during medical school and his loyalty to the *Norfolk Medical News*. He saw the *News* both as a potentially important signpost on the road organized medicine must travel and as a scourge for wrongdoers, and strove to make it fulfill both these missions.

These are medicine's contacts with this outstanding man. More important, perhaps, was the place he occupied in the life of his home town and in Norwood Hospital. Here he was the "old fashioned" family doctor par excellence, beloved by succeeding generations of patients, contributing more than he ever received of material things, but being paid in other ways that he may never have realized and certainly did not seek.

In appreciation of his worth a Dean S. Luce Memorial Fund has already been set up for the benefit of the Norwood Hospital, and a resolution from Norfolk District presented at the last meeting of the Council will, if finally accepted, provide a Dean S. Luce Lectureship in General Practice to be given annually at the May meeting of the Massachusetts Medical Society.

B. E. B.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR APRIL, 1953

Résumé

Disease	April 1953	April 1952	Seven-Year Median
Chancroid	8	2	2
Chicken pox	3529	1826	1826
Diphtheria	8	17	17
Dog bite	1158	1354	1216
Dysentery, bacillary	37	0	7
Encephalitis, infectious	1	6	2
German measles	1190	3431	266
Gonorrhea	187	125	249
Granuloma inguinale	0	0	0
Hepatitis, infectious	192	13	10†
Lymphogranuloma venereum	0	0	1
Malaria	0	9	3
Measles	413	8579	3921
Meningitis, meningococcal	6	5	6
Meningitis, Pfeiffer bacillus	3	6	3
Meningitis, pneumococcal	3	3	2
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	1	2	0
Meningitis, undetermined	10	5	3
Mumps	1504	1205	1205
Poliomyelitis	0	2	0
Salmonellosis	25	5	5
Scarlet fever	543*	474	624
Syphilis	98	136	198
Trichinosis	1	2	5
Tuberculosis, pulmonary	183	229	228
Tuberculosis, other forms	11	22	16
Typhoid fever	4	3	3
Undulant fever	2	0	3
Whooping cough	103	120	281

*Includes streptococcal sore throat.
†Four-year median.

Comment

Diseases below the seven-year median included diphtheria, measles, scarlet fever and whooping cough.

Although the number of reported cases of diphtheria was far below the seven-year median, it was considerably above that of recent months.

The 413 and 120 cases of measles and whooping cough, respectively, represented the lowest figures for these diseases for the month of April in the history of this state.

Diseases above the seven-year median comprised chicken pox, bacillary dysentery, German measles, mumps and salmonellosis.

Chicken pox and bacillary dysentery established new records for the month of April in this state, 3529 and 37 cases, respectively, being reported.

Although the 1190 cases of German measles reported represented a figure above the seven-year median, it fell far short of the 3434 cases reported in April, 1952.

Geographical Distribution of Certain Diseases

The following diseases were reported from the communities named:

Anthrax: Needham, 1.

Diphtheria: Boston, 2; Brockton, 1; Fall River, 1; Lawrence, 1; Somerville, 2; Wilmington, 1; total, 8.

Dysentery, bacillary: Boston, 1; Brookfield, 1; Cambridge, 1; Fitchburg, 1; Holyoke, 1; Leominster, 5; Worcester, 18; Wrentham, 9; total, 37.

Encephalitis, infectious: Leominster, 1.

Hepatitis, infectious: Belchertown, 113; Boston, 11; Brockton, 2; Cambridge, 3; Chicopee, 1; Fort Devens, 4; Haverhill, 1; Holyoke, 1; Lowell, 1; Marlboro, 3; Millbury, 6; Montague, 1; Newton, 1; Pittsfield, 1; Scituate, 1; Somerset, 1; Springfield, 1; Sutton, 1; Worcester, 29; Wrentham, 10; total, 192.

Lymphocytic choriomeningitis: Haverhill, 1.

Meningitis, meningococcal: Boston, 1; Fall River, 1; New Bedford, 1; Springfield, 1; Stoughton, 1; Worcester, 1; total, 6.

Meningitis, Pfeiffer bacillus: Medford, 1; Quincy, 1; Webster, 1; total, 3.

Meningitis, pneumococcal: Boston, 2; Stoughton, 1 ;total, 3.

Meningitis, streptococcal: Worcester, 1.

Meningitis, undetermined: Braintree, 1; Boston, 1; Brockton, 1; Chicopee, 1; Foxboro, 1; Lowell, 1; Mansfield, 1; Quincy, 1; Shelburne, 2; total, 10.

Salmonellosis: Boston, 5; Brockton, 2; Cambridge, 3; Everett, 1; Fall River, 1; Lawrence, 1; Melrose, 3; Quincy, 1; Saugus, 1; Springfield, 2; Waltham, 1; Wayland, 2; Worcester, 2; total, 25.

Tetanus: Lawrence, 1.

Trichinosis: Boston, 1.

Typhoid fever: Lawrence, 2; Newton, 1; Springfield, 1; total, 4.

Undulant fever: Framingham, 1; Holden, 1; total, 2.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

The June schedule of the Consultation Clinics for Crippled Children in Massachusetts is as follows:

Orthopedic Clinic	Date	Clinic Consultant
Salem	June 1	Paul W. Hugenberger, M.D.
Gardner	June 2	Carter R. Rowe, M.D.
Haverhill	June 3	William T. Green, M.D.
Greenfield	June 4	Charles L. Sturdevant, M.D.
Lynn*	June 8	Daniel M. Killoran, M.D., and John J. Crowley, M.D.
Brockton	June 11	George W. Van Gorder, M.D.
Lowell	June 12	Albert H. Brewster, M.D.
Springfield	June 16	James D. Fisher, M.D.
Pittsfield	June 17	Edward J. Coughlin, Jr., M.D.
Fall River	June 22	David S. Grice, M.D.
Hyannis	June 25	Paul L. Norton, M.D.
Worcester	June 26	John W. O'Meara, M.D.

Rheumatic-Fever Clinic	Dates
North Reading	June 2, 9, 16, 23, 30
Fitchburg	June 3, 10, 17, 24

Plastic Clinic	Held	Consultant
Eastern Massachusetts	Semi-monthly	Bradford Cannon, M.D.
Western Massachusetts	Monthly	Joseph M. Baker, M.D.

Physicians referring new patients to clinic should get in touch with the district health officer to make appointments. Patients are seen by appointment only.

*This clinic serves Lynn, Lynnfield, Saugus, Nahant, Revere, Chelsea, Everett and Winthrop. Referrals should be made directly to the Lynn Hospital.

CORRESPONDENCE

NORFOLK DISTRICT MEDICAL SOCIETY

May 14, 1953

To the Editor: The attention of all readers of the *Journal* is invited to the following resolution adopted by the Norfolk District Medical Society at its annual meeting on April 28, 1953: "Resolved, that the Norfolk District Medical Society declares that the *Norfolk Medical News* is not its official organ or publication."

This notice should serve to correct the impression currently held by many readers of the *News*, whether or not members of Norfolk District, that the periodical reflects the views of the Society.

Thomas R. Goethals, M.D.
President
Boston

AUT DORLAND, AUT NULLUS

To the Editor: The title of an article in the April 30 issue of the *Journal* is "Nevus unius lateralis." This looks like Latin, but is it? Can you translate it?

Among the references is a 1941 article by Pack and Sunderland with the title "Naevus unius lateris." This *is* Latin, meaning "nevus of one side," an appropriate name for the entity in question. And it is a pity if one spoils good Latin by not pronouncing it Nae'vus uni'us lat'eris.

Your author notes the myriad of synonyms. With ten thousand at hand, why not choose one that is good Latin, or else good English?

Medical dictionaries, alas, sometimes misguide us. The 1951 *American Illustrated Medical Dictionary* has an entry for the dubious nevus unius lateralis, but disqualifies itself as an arbiter of Latin terminology by incorrectly placing the stress on the first syllable of "unius," and the definition surely pertains to something quite different from naevus unius lateris, which has no entry at all.

HARRY K. MESSENGER, M.D.

Boston

To the Editor: N. Lenson reports in the April 30 issue of the *Journal* another interesting case of unilateral, widespread nevus combined with other changes.

The term "nevus unius *lateralis*," which is used as caption as well as through the entire article, is not correct. The correct term is "nevus unius *lateris*." Lateris is the genitive of latus (Latin) = side. The incorrect term is also to be found in Ormsby-Montgomery, *Diseases of the Skin*, seventh edition (Philadelphia: Lea and Febiger, 1948). Besides nevus unius lateris the synonym nevus unilateralis may be used correctly.

The reader of Lenson's article will learn that reference 1 on page 759 gives the correct term, nevus unius lateris. Lenson describes in the first sentence of his paper nevus unius lateris as an entity, characterized by a congenital papillary growth. It is still a controversial issue whether or not any nevus is of congenital origin. The unilateral nevus need not be a papillary growth. It may consist either of macular, pigmented lesions or papular lesions, or of a combination of macular and papular lesions. Hair and other structures may also compose a unilateral nevus.

ALFRED HOLLANDER, M.D.

Springfield, Massachusetts

To the Editor: Regarding the article by Lenson entitled "Nevus Unius Lateralis," in the April 30 issue of the *Journal*, I should like to mention the following: unus, genitive unius, means one; latus, genitive lateris, means the side; nevus unius lateris is a mole occurring on one side (of the body); and unilateralis means onesided and is obviously an adjective.

It is a linguistic impossibility to combine one adjective (unius) with a second adjective (lateralis). The correct way is nevus unius lateris, and the fact that leading textbooks on dermatology use the wrong name is no excuse to perpetrate the dreadful spelling.

I wish to add that I learn much more from the *Journal* than I have to object to.

JAN SCHWARZ, M.D.

Cincinnati, Ohio

Note: The title of the article in question was originally "Nevus Unius Lateris" and was changed to agree with the usage given in Dorland's *American Illustrated Medical Dictionary*. — ED.

TUBERCULOSIS IN MEDICAL STUDENTS

To the Editor: I wish to commend the *Journal* for presenting in its widely read pages the important article on tuberculosis in American medical students by Abruzzi and Hummel. This study is the work of the Committee on Medical Student Welfare of the Association of Internes and Medical Students, of which Dr. Abruzzi was chairman during his senior year at Columbia and his internship. Several years of work went into the study, which conclusively demonstrates the higher incidence of tuberculosis among medical students and the favorable results that control programs (including BCG) exert on this figure. I am hopeful that the publication of this report will result in control programs at the many schools where they do not as yet exist.

As yet no survey has been attempted to determine the incidence of tuberculosis among house-staff members. This would be a difficult task. It is safe to assume, nevertheless, that such a study would find more tuberculosis among the house staff than among medical students and that control programs should likewise be instituted.

It takes no great feat of imagination to understand what contracting tuberculosis means to a medical student. Aside from the time lost from studies and the limitation of his future activities, the student suffers considerable financial loss. Our organization has recognized this and intends to explore the possibility of tuberculosis insurance for the medical student. Insurance could not be obtained before completion of this survey since the degree of risk had not been calculated and consequently no insurance company could be expected to provide coverage.

HERBERT G. ROSE
National President
Association of Internes and Medical Students

Chicago

NARCOTIC REGISTRATION

To the Editor: Physicians licensed to prescribe narcotics will have received the mimeographed letter that was sent out on May 22 in connection with the renewal of narcotic registration for the coming fiscal year.

To comply with the provisions of the Harrison Narcotic Act, the application and inventory forms must be executed and returned to the Internal Revenue Office, 174 Ipswich Street, Boston, on or before July 1, with remittance covering the tax. Where returns are not filed within the time prescribed by law, the penalties provided become applicable.

Persons who do not contemplate renewing their registration for the coming fiscal year should notify the office of Director Scanlon before July 1, since it is necessary that proper steps be taken to dispose of their supply of narcotics and that all unused narcotic order blanks on hand be returned for the purpose of cancellation.

CHESTER H. CLARK
Chief, Narcotic Section

Office of the Director of Internal Revenue

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Human Embryology (Prenatal Development of Form and Function). By W. J. Hamilton, M.D., D.Sc., F.R.S.E., professor of anatomy in the University of London at Charing Cross Hospital Medical School; J. D. Boyd, M.A., M.Sc., M.D., professor of anatomy, University of Cambridge, and fellow of Clare College; and H. W. Mossman, M.S., Ph.D., associate professor of anatomy, University of Wisconsin Medical School. Second edition. 8°, cloth, 432 pp., with 433 illustrations and 5 tables. Baltimore: Williams and Wilkins, 1952. $9.00.

In this new edition the author has extensively rewritten the whole text, and many of the chapters have been rewritten. Brief introductory statements have been prefixed to the various chapters. The number of pages of text has been increased by 60 and the illustrations by 69. Lists of references are appended to the chapters, and there is a good index. The publishing is excellent in every way. The book was first published in 1947, and reprinted twice before the publication of this second edition.

The Psychoanalytic Study of the Child: Volume VII. Managing editors, Ruth S. Eissler, M.D., Anna Freud, LL.D., Heinz Hartmann, M.D., and Ernst Kris, Ph.D. 8°, cloth, 448 pp., with 4 figures, 2 plates and 1 table. New York: International Universities Press, Incorporated, 1952. $7.50.

This seventh volume in a standard series maintains the high standard of publication. The first part of the text is devoted to 4 papers on the mutual influences in the development of the Ego and Id, read at a symposium held at the seventeenth congress of the International Psycho-Analytical Association, Amsterdam, Holland, August 8, 1951. This is followed by 17 papers on various aspects of child psychoanalysis. A table of contents of the previous 6 volumes is appended to the text. The series should be in all collections on psychoanalysis.

The Unipolar Electrocardiogram: A clinical interpretation. By Joseph M. Barker, M.D., cardiologist, Yater Clinic, associate professor of clinical medicine and special lecturer in physiology, Georgetown University School of Medicine, director of the Heart Station and visiting physician, Georgetown University Hospital, chief of cardiology, Providence Hospital, visiting physician, Gallinger Municipal Hospital, and consulting cardiologist, Arlington Hospital, Arlington, Virginia. Assisted by Joseph J. Wallace, M.D., and advised by Wallace M. Yater, M.D. With a foreword by Frank N. Wilson, M.D. 8°, cloth, 655 pp., with 458 illustrations. New York: Appleton-Century-Crofts, Incorporated, 1952. $12.50.

The author of this new book has endeavored to produce a comprehensive but relatively simple treatment of the unipolar electrocardiogram. He has translated as far as possible mathematical formulas and terminology into prose form in the process of simplification. He has presented and analyzed a great many tracings taken from his own patients. Numerous original line drawings supplement the text. Although unipolar electrocardiography deals primarily with the ventricular complex, a section on the arrhythmias is included. A bibliography of 13 pages is appended to the text; there is a good index, and the publishing is excellent. The book, which presents the views of the author gained from long experience, should be in collections on the subject.

Monographs in Medicine: Series 1. Edited by William B. Bean, M.D., professor of medicine and head, Department of Medicine, State University of Iowa College of Medicine. Assisted by Morton Hamburger, M.D., associate professor of medicine, University of Cincinnati School of Medicine; John A. Leutscher, Jr., M.D., associate professor of medicine, Stanford University School of Medicine; and Stewart Wolk, M.D., professor of medicine and head, Department of Medicine, University of Oklahoma School of Medicine. 8°, cloth, 655 pp., with illustrations. Baltimore: Williams and Wilkins, 1952. $12.00.

This first volume of a new series contains 15 articles on various aspects of medicine, written by 20 physicians. The subjects covered include history taking, precordial sounds, physiology of body fluids, angiocardiography, portal hypertension, pheochromocytoma, respiratory failure in neuromuscular disorders, cortisone and ACTH in infections, prevention of rheumatic fever, amebiasis, chemotherapy of malaria, the seasonal, arthropod-borne, virus encephalitides, sickle-cell anemia, the growth and maturation of the erythrocyte and chemical agents used in the treatment of inoperable and far-advanced neoplastic diseases. Extensive bibliographies are appended to the various articles, which constitute surveys of present-day knowledge of the subjects. There is a good index, and the publishing is excellent. The use of a paper of lighter weight would have made for easier handling. The volume is recommended for all medical libraries.

A Method of Anatomy: Descriptive and deductive. By J. C. Boileau Grant, M.C., M.B., Ch.B., F.R.C.S. (Edin.) professor of anatomy, University of Toronto. Fifth edition. 4°, cloth, 870 pp., with 862 illustrations. Baltimore: Williams and Wilkins, 1952. $7.00.

This standard textbook on anatomy has enjoyed an unusual publication history during the past fifteen years. First published in 1937, it has gone through 16 printings of five editions to date. The type and printing are good, and the paper is light in weight. There is a comprehensive index.

First International Symposium on Chemical Microbiology: Microbial growth and its inhibition. 8°, paper, 285 pp., with 67 illustrations and 38 tables. Geneva: World Health Organization, 1952. $3.00. (*World Health Organization Monograph Series No. 10.*)

The first international symposium on chemical microbiology was held in Rome, June 25–30, 1951. A large number of scientists from many parts of the world participated in the meetings, and 18 papers were read and discussed on various aspects of the subject, ranging from the physiologic principles underlying the antagonism between certain micro-organisms and antibiotic substances to a description of the new laboratory technics of antibiotic production. The papers are given in the language of the authors, English and French, with résumés in both languages. Lists of references are appended to the papers. The monograph should be in all collections on the subject.

A Manual of Orthoptics. By Julia E. Lancaster, M. A., San Francisco Ophthalmic Laboratory, San Francisco, California. 8°, cloth, 199 pp. Springfield, Illinois: Charles C Thomas, 1951. $5.50.

This manual emphasizes diagnosis and treatment. The fundamentals of optics, anatomy, physiology and the diagnosis of neuromuscular anomalies of the eyes are purposely omitted. The subject is primarily concerned with the treatment of strabismus and the improvement of binocular vision. The text is divided into two parts on orthoptic problems and on technics. There is a good index. The book should prove of value to ophthalmologists.

Pardon My Sneeze. By Milton Millman, M.D. 8°, paper, 217 pp., with 15 illustrations. San Diego, California: Frye and Smith, Limited, 1952.

This book written for the laity discusses allergic diseases in their various aspects.

Great Adventures in Medicine. Edited by Samuel Rapport and Helen Wright. With an introduction by Detlev W. Bronk, president of Johns Hopkins University. 8°, cloth, 874 pp. New York: The Dial Press, 1952. $5.00.

The editors of this compilation have gathered from various sources exerpts of contributions by authorities on various aspects of medicine. Beginning with the oath of Hippocrates and ending with the present time, the material is divided into five periods. After an introduction, the subjects include the ancient and medieval times, the rebirth of medicine, into modern times in both the old and new worlds, the turn of the century and beyond, and contemporary medicine. There is an index and the publishing is good. The book should be in all medical-history collections in all libraries.

Physiology of the Eye: Vision. Volume two. By Arthur Linksz, M.D., assistant clinical professor of ophthalmology, New York University Postgraduate School of Medicine, and associate attending surgeon, Manhattan Eye, Ear and Throat Hospital, New York City. 4°, cloth, 869 pp., with 24 illustrations. New York, New York: Grune and Stratton, 1952. $19.00.

Dr. Linksz presented *Optics*, the first volume of his projected series on the *Physiology of the Eye*, in 1950. This second of the series is devoted to vision and is divided into four parts: analysis of sensation, patterns and detail vision, the perception of spatial relations, and vision and the oculorotary reflexes. A bibliography and indexes of authors and subjects are appended to the text. The publishing is good, and the set should be in reference collections on the eye.

A 40 Year Campaign Against Tuberculosis. By Louis I. Dublin, Ph.D., second vice-president and statistician, Metropolitan Life Insurance Company. 8°, cloth, 115 pp., with illustrations, 4 charts and 8 tables. San Francisco: Metropolitan Life Insurance Company, 1952.

The Metropolitan Life Insurance Company has successfully worked for the control of tuberculosis for four decades. When the work began, about 5,000,000 persons were insured, in addition to 15,000 employees. In 1914 the Mount McGregor Sanatorium in the Adirondacks was established, and in 1917 the well known Framingham demonstration was inaugurated. The history of both these events is given in detail. A list of references is appended to the text. An index of names at least would have made the book more valuable. This short history tells the story of a great achievement in preventive medicine by a great commercial organization.

Physiological Bases of Gynecology and Obstetrics. By S. R. M. Reynolds, M.A., Ph.D., D.Sc., staff member, physiologist, Department of Embryology, Carnegie Institution of Washington, and lecturer in obstetrics, Johns Hopkins University School of Medicine. 8°, cloth, 153 pp. Springfield, Illinois: Charles C Thomas, 1952. $5.50. (Publication No. 128, *American Lecture Series.*)

The 15 lectures in this book are part of a larger course on the postgraduate level for physicians at the Facultad de Medicina de Montevideo. They discuss various topics in the fields of obstetrics and gynecology. A supplementary reading list for the various lectures is appended to the text, and there is a good index.

Finality and Form. By Warren S. McCulloch, M.D., professor of psychiatry and physiology and neurophysiologist, Department of Psychiatry, University of Illinois College of Medicine and Illinois Neuropsychiatric Institute. 8°, cloth, 63 pp., with 25 illustrations. Springfield, Illinois: Charles C Thomas, 1952. $3.75. (Publication No. 111, *American Lecture Series.*)

In this small monograph Dr. McCulloch discusses in a diagrammatic manner the evolution of the brain.

Progress in Fundamental Medicine. Edited by J. F. A. McManus, M.D., University of Virginia. 4°, cloth, 316 pp., with 74 illustrations and 2 colored plates. Philadelphia: Lea and Febiger, 1952. $9.00.

This joint work by 10 distinguished physicians discusses and brings up to date the knowledge on the following topics: parenteral nutrition, with particular reference to protein hydrolysates; melanotic tumors of the skin; pathology of systemic lupus erythematosus; diagnosis of fungous infections and staining methods; the liver; a survey of technics for the histochemical approach to pathology; coronary-artery disease; the problem of carcinoma in situ with reference to the human cervix uteri; recognition of carcinoma in situ of the cervix uteri by Papanicolaou's method; and nonsilica pneumonoconioses. Extensive bibliographies are appended to the articles, and there is an index. The publishing is good. This is a type of book for all medical libraries.

The Moral Theory of Behavior: A new answer to the enigma of mental illness. By Frank R. Barta, M.D., director, Department of Psychiatry and Neurology, Creighton University School of Medicine and St. Joseph's Creighton Memorial Hospital, Omaha. 8°, cloth, 35 pp., with 3 illustrations. Springfield, Illinois: Charles C Thomas, 1952. $2.00. (Publication No. 163, *American Lecture Series.*)

Dr. Barta discusses the philosophic, psychologic and clinical aspects of mental illness and its nature, treatment and prognosis. A short list of references and a good index conclude the monograph.

An Introduction to Medical Sciences: An elementary text on pathology. By William Boyd, M.D., Dipl. Psych., M.R.C.P. (Edin.), F.R.C.P. (London), F.R.C.S. (Canada), LL.D. (Sask.), M.D. (Oslo), F.R.S. (Canada), professor of pathology, University of British Columbia, Vancouver. Fourth edition. 8°, cloth, 304 pp., with 124 illustrations and 3 colored plates. Philadelphia: Lea and Febiger, 1952. $4.50.

This new edition of a well known monograph has been thoroughly revised and brought up to date. The most important changes have been made in the sections on treatment. Material on the antibiotics, the sulfonamides, cortisone and ACTH has been added. The text is divided into three parts: general principles, the organs and their diseases, and practical applications. There is a good index; the publishing is good.

Essentials of Body Mechanics in Health and Disease. By Joel E. Goldthwait, M.D., LL.D., Sc.D., Lloyd T. Brown, M.D., Loring T. Swaim, M.D., and John G. Kuhns, M.D., Sc.D. Fifth edition. 12°, cloth, 355 pp., with 135 illustrations. Philadelphia: J. B. Lippincott Company, 1952. $6.00.

This well known manual has been revised and brought up to date. Lists of references are appended to the chapters; there is a good index; and the publishing is excellent. The book should be in collections on orthopedics.

Nutrition and Diet in Health and Disease. By James S. McLester, M.D., and William J. Darby, M.D., Ph.D., professor of biochemistry and director, Division of Nutrition, Vanderbilt University School of Medicine. Sixth edition. 8°, cloth, 710 pp., with 145 tables. Philadelphia: W. B. Saunders Company, 1952. $10.00.

In this sixth edition of a standard book Dr. McLester has for the first time acquired the assistance of a collaborator, Dr. Darby, who has assumed responsibility for the first part on nutrition in health. Dr. McLester has written the second part on nutrition in disease. The text has been revised and brought up to date since the publication of the previous edition in 1949. The bibliographies, which have likewise been revised to include the recent literature of importance, nevertheless retain the classic references and useful reviews. The publishing is excellent. The book is recommended for all medical libraries.

Post-Graduate Lectures on Orthopedic Diagnosis and Indications. Vol. 4. By Arthur Steindler, M.D., professor of orthopedic surgery, State University of Iowa College of Medicine, Iowa City. 4°, cloth, 31 pp., with 275 illustrations. Springfield, Illinois: Charles C Thomas, 1952. $9.75.

This new volume of an important series discusses the various aspects of arthritis and diseases of muscles, bursas, tendons and fasciae, and deficiency and degenerative diseases of the locomotor system. The complete series should be in all orthopedic collections.

Infrared Photography in Medicine. By Leo C. Massopust, Sr., director, Department of Art and Photography, Marquette University School of Medicine, Milwaukee. 8°, cloth, 53 pp., with 31 illustrations. Springfield, Illinois: Charles C Thomas, 1952. $2.75. (Publication No. 152, *American Lecture Series.*)

This monograph discusses briefly the uses of infrared photography in medicine. The chapters are devoted to materials and methods, and applications. There are also chapters on the infrared procedure in photomicrography and on the superficial venous system. The book is well illustrated, and there is a list of references and an index.

Diseases of Metabolism: Detailed methods of diagnosis and treatment. Edited by Garfield G. Duncan, M.D., director, Medical Division, Pennsylvania Hospital, and clinical professor of medicine, Jefferson Medical College, Philadelphia. Third edition. 8°, cloth, 1179 pp., with illustrations. Philadelphia: W. B. Saunders Company, 1952. $15.00.

Twenty collaborators have thoroughly revised and in part rewritten this standard book to bring it up to date since the publication of the previous edition of 1947. A chapter on porphyrin metabolism has been added. The pertinent literature has been surveyed throughout the text, and lists of references have been appended to the chapters. There are extensive indexes of authors and subjects. The book is recommended for all medical libraries.

Kitchen Strategy. By Leona M. Bayer, M.D., assistant clinical professor of medicine, Stanford University School of Medicine, San Francisco; and Edith Green, television cooking expert, San Francisco. 8°, paper, 94 pp., with illustrations. Springfield, Illinois: Charles C Thomas, 1952. $3.75.

This is a practical manual on cookery and diet, written by two specialists in their particular fields.

NOTICES

NEW ENGLAND CENTER HOSPITAL HOUSE OFFICERS' ASSOCIATION

The House Officers' Association of the New England Center Hospital announces the following program in its Evening Lecture Series, to be held in the Stearns Auditorium of the New England Center Hospital, on Friday, June 12, at 7 p.m.:

Remarks on the Philosophy of Psychotherapy. Dr. Frieda Fromm-Reichmann, director of psychotherapy, Chestnut Lodge Sanitarium, Rockville, Maryland.

The discussers will be Drs. Bernard Bandler and Justin Hope.

All interested persons are cordially invited to attend.

SOCIETY MEETINGS AND CONFERENCES

JUNE 7-9. American College of Cardiology. Page 395, issue of February 26.

JUNE 10-13. American Proctologic Society. Page 746, issue of April 23. Notice above.

JUNE 12. New England Center Hospital House Officers' Association. Notice above.

JUNE 15-17. American Neurological Association. Page 836, issue of May 7.

JUNE 26-28. American Academy of Dental Medicine. Page 664, issue of April 9.

JUNE 28-July 2. American Society of X-Ray Technicians. Page 480, issue of March 12.

JULY 8 AND 9. Seventh Annual Rocky Mountain Cancer Conference. Page 644, issue of April 9.

AUGUST 18-21. Third International Congress of Electroencephalography and Clinical Neurophysiology. Page 707, issue of April 16.

OCTOBER 28. New England Obstetrical and Gynecological Society. Page 868, issue of November 27.

(*Notices concluded on page xv*)